

=> fil reg

FILE 'REGISTRY' ENTERED AT 11:24:46 ON 08 AUG 2002

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STRUCTURE FILE UPDATES: 7 AUG 2002 HIGHEST RN 443093-92-3

DICTIONARY FILE UPDATES: 7 AUG 2002 HIGHEST RN 443093-92-3

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que l36

L21 STR

10  
S  
~  
C  
@8

N~G1~S~G2~G1~N  
1 2 3 4 5 6

REP G1=(0-1) 8

REP G2=(1-5) S

NODE ATTRIBUTES:

NSPEC IS RC AT 1

NSPEC IS RC AT 6

CONNECT IS M1 RC AT 1

CONNECT IS M1 RC AT 6

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED

NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

L23 , SCR 1993 AND 2022

L24 SCR 2043 OR 2050 OR 2049 OR 2054 OR 2039

L26 1270 SEA FILE=REGISTRY SSS FUL L21 AND L23 NOT L24

L27 STR

N~S~G2~N

1 2 3 4

REP G2=(1-5) S

NODE ATTRIBUTES:

NSPEC IS RC AT 1

NSPEC IS RC AT 4

CONNECT IS M1 RC AT 1

CONNECT IS M1 RC AT 4

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

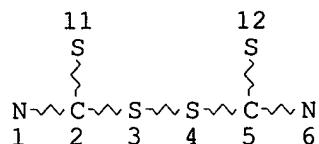
GRAPH ATTRIBUTES:

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
[jan.delaval@uspto.gov](mailto:jan.delaval@uspto.gov)

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 4

STEREO ATTRIBUTES: NONE

L29 513 SEA FILE=REGISTRY SUB=L26 CSS FUL L27  
L30 STR



NODE ATTRIBUTES:

NSPEC IS RC AT 1  
NSPEC IS RC AT 6  
CONNECT IS M1 RC AT 1  
CONNECT IS M1 RC AT 6  
DEFAULT MLEVEL IS ATOM  
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RING(S) ARE ISOLATED OR EMBEDDED  
NUMBER OF NODES IS 8

STEREO ATTRIBUTES: NONE

L32 635 SEA FILE=REGISTRY SUB=L26 CSS FUL L30  
L36 1148 SEA FILE=REGISTRY ABB=ON PLU=ON (L29 OR L32)

=> d his

(FILE 'HOME' ENTERED AT 10:04:46 ON 08 AUG 2002)  
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 10:04:55 ON 08 AUG 2002

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      E WO99-AU724/AP, PRN
L1      1 S E3, E4
      E BERNARD H/AU
L2      118 S E3, E10, E15-E17
      E TAN Y/AU
L3      91 S E3, E10
      E TAN YEE/AU
L4      14 S E4
      E BEERHEIDE W/AU
L5      8 S E3, E4
      E TING A/AU
L6      86 S E3, E5
L7      20 S E26, E27
      E SIM M/AU
L8      9 S E3, E10
L9      19 S E31
      E PAPILLOMAVIRUS/CT
      E E3+ALL
L10     5802 S E6, E5+NT
L11     14774 S E4+NT
L12     9994 S ?PAPILLOM?
L13     5007 S HPV? OR MPV?
L14     50 S L2-L9 AND L10-L13
L15     1 S L1 AND L14
L16     49 S L14 NOT L15
L17     2 S L16 AND ?DISULF?
L18     3 S L15, L17

```

SEL RN

FILE 'REGISTRY' ENTERED AT 10:13:43 ON 08 AUG 2002

L19 105 S E1-E105  
L20 80 S L19 AND (N AND S)/ELS  
L21 STR  
L22 1 S L21 CSS  
L23 SCR 1993 AND 2022  
L24 SCR 2043 OR 2050 OR 2049 OR 2054 OR 2039  
L25 7 S L21 AND L23 NOT L24  
L26 1270 S L21 AND L23 NOT L24 FUL  
SAV L26 KWON763/A  
L27 STR L21  
L28 28 S L27 CSS SAM SUB=L26  
L29 513 S L27 CSS FUL SUB=L26  
SAV L29 KWON763A/A  
L30 STR L21  
L31 28 S L30 CSS SAM SUB=L26  
L32 635 S L30 CSS FUL SUB=L26  
SAV L32 KWON763B/A  
L33 49 S L20 AND L29,L32  
L34 31 S L20 NOT L33  
L35 STR L21  
L36 1148 S L29,L32  
L37 39 S L35 CSS SAM SUB=L36  
L38 STR L35  
L39 48 S L38 CSS SAM SUB=L36  
L40 9 S L39 NOT L37  
L41 1007 S L38 CSS FUL SUB=L36  
L42 141 S L36 NOT L41

FILE 'HCAPLUS' ENTERED AT 11:18:48 ON 08 AUG 2002

L43 8760 S L41  
L44 98 S L42  
L45 2830 S L33  
L46 8834 S L43-L45  
L47 3 S L2-L9 AND L46  
L48 12 S L10-L13 AND L46  
L49 12 S L47,L48  
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 11:24:02 ON 08 AUG 2002

L50 50 S E106-E155

FILE 'REGISTRY' ENTERED AT 11:24:46 ON 08 AUG 2002

=&gt; fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:25:07 ON 08 AUG 2002

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FILE COVERS 1907 - 8 Aug 2002 VOL 137 ISS 6  
 FILE LAST UPDATED: 7 Aug 2002 (20020807/ED)

This file contains CAS Registry Numbers for easy and accurate  
 substance identification.

CAS roles have been modified effective December 16, 2001. Please  
 check your SDI profiles to see if they need to be revised. For  
 information on CAS roles, enter HELP ROLES at an arrow prompt or use  
 the CAS Roles thesaurus (/RL field) in this file.

=> d 149 all tot

L49 ANSWER 1 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:157589 HCAPLUS

DN 136:210549

TI Retinol binding protein receptor-related treatment of hyperproliferative  
 diseases

IN Ward, Simon; Bavik, Claes; Cork, Michael; Tazi-Ahnini, Rachid

PA University of Sheffield, UK

SO PCT Int. Appl., 139 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K038-00

CC 1-6 (Pharmacology)

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002015920	A2	20020228	WO 2001-GB3694	20010817
	W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			
	AU 2001078632	A5	20020304	AU 2001-78632	20010817
PRAI	GB 2000-20351	A	20000817		
	WO 2001-GB3694	W	20010817		
AB	Methods and comps. are provided for treating a patient suffering from a hyperproliferative disorder or photoageing. The methods involve blocking the activity of a retinol binding protein receptor (RBPr) in cells of the patient, and/or administering to the patient an antagonist of a retinol binding protein receptor (RBPr) and/or lowering the endogenous level of retinoic acid (RA) in cells of said patient.				
ST	retinol binding protein receptor hyperproliferative disease photoaging treatment; retinoic acid redn hyperproliferative disease photoaging treatment				
IT	Keratins				
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (1; retinol binding protein receptor-related treatment of hyperproliferative diseases)				
IT	Skin, disease				
	(Darriers disease; retinol binding protein receptor-related treatment of hyperproliferative diseases)				
IT	Peroxisome proliferator-activated receptors				
	RL: BSU (Biological study, unclassified); BIOL (Biological study) (PPAR response element; retinol binding protein receptor-related treatment of hyperproliferative diseases)				
IT	Genetic element				

RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (RARE (retinoic acid-responsive element); retinol binding protein  
 receptor-related treatment of hyperproliferative diseases)

IT Receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (RBP (retinol binding protein); retinol binding protein  
 receptor-related treatment of hyperproliferative diseases)

IT Genetic element  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (TRE (thyroid hormone-responsive element); retinol binding protein  
 receptor-related treatment of hyperproliferative diseases)

IT Keratosis  
 (actinic; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Mental disorder  
 (affective, seasonal; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Antiarteriosclerotics  
 (antiatherosclerotics; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Bone, disease  
 (bone growth disorder; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Kidney, neoplasm  
 (carcinoma, inhibitors; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Lupus erythematosus  
 (cutaneous; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Angiogenesis  
 Fertility  
 Spermatogenesis  
 (disorder; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Skin, disease  
 (epidermal naevoid syndromes; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Skin  
 (epidermis, enhanced or compromised epidermal barrier function; retinol  
 binding protein receptor-related treatment of hyperproliferative  
 diseases)

IT Keratosis  
 (epidermolytic hyperkeratosis; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Skin, disease  
 (erythrokeratoderma variabilis; retinol binding protein  
 receptor-related treatment of hyperproliferative diseases)

IT Bone, disease  
 (fracture; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Toxicity  
 (hepatotoxicity; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Keratosis  
 (hyper-, palmoplantar; retinol binding protein receptor-related  
 treatment of hyperproliferative diseases)

IT Keratosis  
 (hyperkeratosis; retinol binding protein receptor-related treatment of  
 hyperproliferative diseases)

IT Skin, disease  
 (hypertrophic scar; retinol binding protein receptor-related treatment  
 of hyperproliferative diseases)

IT Skin, disease

(ichthyosis; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Egg  
(implantation, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Cell differentiation  
(inducers; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(irritation; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin  
(keratinization, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin  
(keratinocyte; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Antitumor agents  
(kidney carcinoma; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(lichen planus; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Melanins  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(melanogenesis disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Antibodies  
RL: BPN (Biosynthetic preparation); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(monoclonal; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(non-bullous ichthyosiform erythroderma; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(photoaging; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(pigmentation, disorder; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Skin, disease  
(pityriasis rubra pilaris; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Surgery  
(post-operative scarring; retinol binding protein receptor-related treatment of hyperproliferative diseases)

IT Alopecia  
Antidepressants  
Antitumor agents  
Antiviral agents  
Cirrhosis  
Cytotoxic agents  
Drug screening  
Fibroblast  
Hepatitis  
Hepatitis C virus  
Human herpesvirus  
Human immunodeficiency virus  
**Human papillomavirus**  
Hypolipemic agents  
Keloid

Psoriasis  
 Wart  
 Wound healing promoters  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Gene, animal  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Antisense DNA  
 Antisense RNA  
 Antisense oligonucleotides  
 Immunoglobulins  
 Peptides, biological studies  
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
 (Biological study); USES (Uses)  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Proteins  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
   (retinol-binding; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Skin, disease  
   (rosacea; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Antitumor agents  
   (squamous cell carcinoma; retinol binding protein receptor-related  
   treatment of hyperproliferative diseases)

IT Osteoporosis  
   (therapeutic agents; retinol binding protein receptor-related treatment  
   of hyperproliferative diseases)

IT Liver  
   (toxicity; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Biological transport  
   (uptake; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT Genetic element  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
   (vitamin D-responsive element; retinol binding protein receptor-related  
   treatment of hyperproliferative diseases)

IT Acne  
   (vulgaris; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT 9031-72-5, Alcohol dehydrogenase   9033-53-8, Retinol dehydrogenase  
 37250-99-0, Retinal dehydrogenase  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
   (isoforms; retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT 68-26-8, Retinol   116-31-4, Retinal   302-79-4, Retinoic acid  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT 401572-74-5  
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological  
 study); USES (Uses)  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT 401572-75-6   401572-76-7  
 RL: PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic  
 use); BIOL (Biological study); USES (Uses)  
   (retinol binding protein receptor-related treatment of  
   hyperproliferative diseases)

IT 97-77-8, Disulfiram 637-03-6, Phenylarsine oxide 5392-40-5,  
3,7-Dimethyl-2,6-octadienal 5697-56-3, Carbenoxolone 7554-65-6,  
4-Methylpyrazole  
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(retinol binding protein receptor-related treatment of  
hyperproliferative diseases)

IT 401890-74-2 401890-75-3  
RL: PRP (Properties)  
(unclaimed nucleotide sequence; retinol binding protein  
receptor-related treatment of hyperproliferative diseases)

L49 ANSWER 2 OF 12 HCAPLUS COPYRIGHT 2002 ACS  
AN 2001:906113 HCAPLUS  
DN 136:25138  
TI Skin patch for use in contact immunotherapy  
IN Hopp, Robert B.  
PA USA  
SO U.S. Pat. Appl. Publ., 15 pp., Cont.-in-part of U.S. Ser. No. 95,700,  
abandoned.  
CODEN: USXXCO

DT Patent  
LA English  
IC ICM A61K039-35  
ICS A61K009-70  
NCL 424449000  
CC 63-6 (Pharmaceuticals)  
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 2001051182	A1	20011213	US 2001-768156	20010125
PRAI	US 1996-717108	A2	19960920		
	US 1998-95700	B2	19980608		

AB A device, preferably in the form of a skin patch, is disclosed for usage  
in the delivery of a contactant to human skin for the purpose of treating  
medical conditions responsive to contact immunotherapy, without the  
presence of medication to alleviate contact dermatitis induced by the  
contactant. The skin patch specifically induces a cell-mediated contact  
dermatitis in the treatment of skin disorders. Its anticipated use  
pertains to treatment of, for example, human **papilloma** virus  
infections, or warts. In a first embodiment, a pressure activated single  
chambered skin patch is topically applied and used for controlled release  
of contactant to human skin. In a second embodiment, a pressure activated  
two-chambered skin patch is topically applied and used for controlled  
release of a contactant to human skin. Alternatively, a single chambered  
skin patch is topically applied and hydrated by the contacted skin for  
release of contactant. In an addnl. embodiment, the contactant may be  
applied sep. of the skin patch portion, in a manner that maintains the  
contactant in contact with the patient's skin for the predetd. period of  
time necessary to cause sufficient contact dermatitis to effect resoln. of  
the medical condition. A single reservoir system for the delivery of  
squaric acid di-Bu ester to the skin was constructed.

ST skin patch contact immunotherapy

IT Balsams  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(Peru; skin patch for use in contact immunotherapy)

IT Alopecia  
(areata; skin patch for use in contact immunotherapy)

IT Synthetic rubber, biological studies  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(black; skin patch for use in contact immunotherapy)



IT Dermatitis  
(contact; skin patch for use in contact immunotherapy)

IT Lymphocyte  
(induction; skin patch for use in contact immunotherapy)

IT AIDS (disease)  
Immunotherapy  
**Papillomavirus**  
Perfumes  
Vitiligo  
(skin patch for use in contact immunotherapy)

IT Epoxy resins, biological studies  
Rosin  
Thiols (organic), biological studies  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(skin patch for use in contact immunotherapy)

IT Drug delivery systems  
(topical; skin patch for use in contact immunotherapy)

IT Drug delivery systems  
(transdermal; skin patch for use in contact immunotherapy)

IT Alcohols, biological studies  
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL  
(Biological study); USES (Uses)  
(wool; skin patch for use in contact immunotherapy)

IT 50-00-0, Formaldehyde, biological studies 54-64-8, Thimerosal 91-22-5,  
Quinoline, biological studies 98-54-4, p-tert-Butylphenol 99-96-7D,  
p-Hydroxybenzoic acid, esters 106-50-3, p-Phenylenediamine, biological  
studies 137-26-8, Thiuram 149-30-4, Mercaptobenzothiazole  
333-18-6, Ethylenediamine dihydrochloride 886-38-4,  
Diphenylcyclopropenone 1405-10-3, Neomycin sulfate 2892-62-8, Squaric  
acid dibutyl ester 4080-31-3, Quaternium 15 7646-79-9, Cobalt  
dichloride, biological studies 7778-50-9, Potassium dichromate  
7786-81-4, Nickel sulfate 25567-67-3, Dinitrochlorobenzene 26172-55-4  
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological  
study); USES (Uses)  
(skin patch for use in contact immunotherapy)

L49 ANSWER 3 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:840664 HCAPLUS

DN 134:110110

TI Inactivation of the human **papillomavirus-16** E6 oncoprotein by  
organic disulfides

AU **Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo**  
**; Bernard, Hans-Ulrich; Ting, Anthony E.**

CS Drug Screen Development Laboratory, Institute of Molecular and Cell  
Biology, Singapore, 117609, Singapore

SO Bioorganic & Medicinal Chemistry (2000), 8(11), 2549-2560  
CODEN: BMECEP; ISSN: 0968-0896

PB Elsevier Science Ltd.

DT Journal

LA English

CC 1-3 (Pharmacology)  
Section cross-reference(s): 21

AB We are investigating compds. that could be useful in the treatment of  
neoplastic lesions of the cervix by acting on the oncoprotein E6 of human  
**papillomavirus-16**. The E6 protein contains two potential  
zinc-binding domains that are required for most of its functions. We have  
published tests that measure (i) the release of zinc ions after chem.  
alteration of the cysteine groups of these zinc-binding domains (TSQ  
assay), (ii) the interaction of E6 with the cellular proteins E6AP and  
E6BP (BIACORE assay), and (iii) the viability of tumor cell lines that  
require the continuous expression of **HPV** oncoproteins (WST1  
assay). Based on these tests, we identified 4,4'-dithiodimorpholine as a

potential lead compd. In this study we examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be an important mol. prerequisite for further drug development in this system. We have evaluated 59 new substances including org. disulfides and those contg. the dithiobisamine moiety, as well as structural analogs. The compds. with significant reactivity in all three assays were obsd. only for dithiobisamine derivs. with satd. cyclic amines and aryl substituted piperazines. The identity of these substances suggests that the N-S-S-N moiety is necessary but not sufficient for reactivity in our assays, and that dithiobisamine based substances are useful as lead compds. that target the cysteine groups of HPV-16 E6 zinc fingers.

- ST disulfide org prepn **papillomavirus** oncoprotein inactivation;  
cervix neoplasm inhibitor org disulfide prepn
- IT Proteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E6; prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT Uterus, neoplasm  
(cervix, inhibitors; prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT Antitumor agents  
(cervix; prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT Human **papillomavirus 16**  
Structure-activity relationship  
(prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT Amines, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(secondary; prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT Protein motifs  
(zinc-binding domain; prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT 729-46-4P 1013-93-0P 1468-28-6P 2129-27-3P  
5328-68-7P 6542-61-6P 7764-30-9P 10220-20-9P  
15575-30-1P 16131-50-3P 17376-42-0P 36903-85-2P  
36938-10-0P 59226-72-1P 62158-06-9P  
72896-38-9P 85865-96-9P 98999-00-9P  
103388-17-6P 260973-66-8P 260973-72-6P  
260973-79-3P 260973-81-7P 260973-83-9P  
260973-85-1P 303796-55-6P 320609-04-9P  
320609-05-0P 320609-06-1P 320609-07-2P  
320609-08-3P 320609-09-4P 320609-10-7P  
320609-11-8P 320609-12-9P 320609-13-0P  
320609-14-1P 320609-15-2P 320609-16-3P  
320609-17-4P 320609-18-5P 320609-19-6P  
320609-21-0P 320609-22-1P 320609-23-2P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of org. disulfides and inactivation of human **papillomavirus-16** E6 oncoprotein)
- IT 103-34-4 120-78-5 880-09-1 1623-84-3  
1623-85-4 2127-10-8 2550-40-5 3256-06-2,  
Thioperoxydicarbonimidic diamide ( $[(H_2N)C(NH)]_2S_2$ ) 5117-07-7  
14193-38-5 15658-35-2 26087-98-9 61747-35-1 66304-01-6  
66546-28-9  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(prepn. of org. disulfides and inactivation of human

**papillomavirus-16 E6 oncoprotein)**

IT 85-46-1, Naphthalene-1-sulfonyl chloride 98-88-4, Benzoyl chloride  
110-91-8, Morpholine, reactions 1122-82-3, Cyclohexyl isothiocyanate  
6160-65-2, 1,1'-Thiocarbonyl diimidazole 7693-46-1, 4-Nitrophenyl  
chloroformate 10025-67-9, Disulfur dichloride  
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of org. disulfides and inactivation of human

**papillomavirus-16 E6 oncoprotein)**

RE.CNT 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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DN 133:79356  
 TI Synthetic and therapeutic methods for the alpha and beta domains of  
 metallothionein  
 IN Vallee, Bert L.  
 PA USA  
 SO PCT Int. Appl., 64 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM A61K009-14  
 ICS A61K009-70; A61K038-17; C07K001-04; C07K001-06; C07K001-16;  
 C07K014-825  
 CC 63-6 (Pharmaceuticals)  
 Section cross-reference(s): 1, 2, 4, 8, 34

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000038654	A1	20000706	WO 1999-US30573	19991221
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			

PRAI US 1998-113459P P 19981223

AB The present invention relates to the alpha and beta domains of metallothionein and analogs thereof, their synthesis, and therapeutic applications of them. Purified metal-free and metal-contg. alpha and beta domains of metallothionein are provided. A high yield method of synthesis and purifn. is also provided for the metal-free and metal-contg. alpha and beta domains of metallothionein. Finally, therapeutic methods are provided that use the alpha and beta domains of metallothionein to transport selected metals to specific tissues or to sequester metals from these tissues in order to treat conditions in those tissues that are ameliorated by the addn. or sequestration of these metals.

ST metallothionein domain metal sequestration tissue targeting

IT Hepatitis

(C; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Protective groups

(CBZ; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Intestine, disease

(Crohn's; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Protective groups

(Fmoc; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Imaging

(NMR, reagents for; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Appetite

(anorexia nervosa; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Antigens

RL: BOC (Biological occurrence); BSU (Biological study, unclassified);

BIOL (Biological study); OCCU (Occurrence)

(antibodies specific for; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Prostate gland

(benign hyperplasia; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Appetite  
(bulimia; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT **Papillomavirus**  
(carcinogenesis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Heart, disease  
(cardiomyopathy; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Drug delivery systems  
(carriers; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Nervous system  
(central, disease; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Intestine, disease  
(colitis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Dialysis  
(complications from kidney-related; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Threads  
Threads  
(cotton, supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Disease, animal  
(deficiency, for metals; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Nervous system  
(degeneration; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Digestive tract  
Endocrine system  
Parathyroid gland  
Skeleton  
(disease; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Circulation  
Immunity  
Vision  
(disorder; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Radiation  
(exposure, disease from; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Proteins, specific or class  
RL: ARU (Analytical role, unclassified); ANST (Analytical study)  
(immobilized; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Human immunodeficiency virus  
(infection; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Drug delivery systems  
(injections, i.v.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Chemotherapy  
(injury from; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Infection  
(measles; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Antibodies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(metallothionein domains bound to; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Prostate gland  
Prostate gland  
(neoplasm, inhibitors; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Nerve, disease  
(neuropathy; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Keratosis  
(parakeratosis; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Apoptosis  
(pathol.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Actinides  
Main group elements  
Rare earth metals, biological studies  
Transition metals, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(peptide domains contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Solid phase synthesis  
(peptide; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Blood vessel, disease  
(peripheral; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Antitumor agents  
(prostate gland; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Eye, disease  
(retinitis pigmentosa; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Metals, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(sequestration of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Chromatography  
Paper  
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Fibers  
Glass beads  
RL: NUU (Other use, unclassified); USES (Uses)  
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Drug delivery systems  
(suppositories; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT Peptides, preparation  
RL: PNU (Preparation, unclassified); PREP (Preparation)  
(synthesis of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

IT AIDS (disease)  
Adrenal gland, disease  
Alcoholism  
Alopecia

Alzheimer's disease  
 Anti-AIDS agents  
 Anti-Alzheimer's agents  
 Anti-inflammatory agents  
 Antiarthritics  
 Anticonvulsants  
 Antidiarrheals  
 Antiobesity agents  
 Antiparkinsonian agents  
 Antitumor agents  
 Antiviral agents  
 Asthma  
 Binders  
 Buffers  
 Common cold  
 Drug delivery systems  
 Drug dependence  
 Drug targeting  
 Emulsifying agents  
 Epilepsy  
 Fluorescent substances  
 Gel permeation chromatography  
 Hemochromatosis  
 Infection  
 Mental disorder  
 Neoplasm  
 Obesity  
 Osteoarthritis  
 Ovary, disease  
 Parkinson's disease  
 Particle size distribution  
 Preparative chromatography  
 Protein motifs  
 Protein sequences  
 Semliki Forest virus  
 Sequestering agents  
 Skin, disease  
 Thyroid gland, disease  
 Transformation, neoplastic  
 Wetting agents  
 Wilson's disease

(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

#### IT Metallothioneins

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

#### IT Radionuclides, biological studies

RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

#### IT Lupus erythematosus

(systemic; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

#### IT Protective groups

(t-Boc; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

#### IT Cotton fibers

Cotton fibers

(threads, supports; synthetic and therapeutic methods for the alpha and

- beta domains of metallothionein)
- IT Muscle, disease  
(white muscle disease of lambs; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT Sheep  
(white muscle disease of; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 100-68-5, Thioanisole 108-95-2, Phenol, uses 7732-18-5, Water, uses 7761-88-8, Silver(I) nitrate, uses 26914-40-9, Ethanedithiol  
RL: NUU (Other use, unclassified); USES (Uses)  
(cleaving soln. contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 106-89-8, Epichlorohydrin, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(dextran crosslinker; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 9004-54-0, Dextran, analysis  
RL: ARU (Analytical role, unclassified); DEV (Device component use); PEP (Physical, engineering or chemical process); ANST (Analytical study); PROC (Process); USES (Uses)  
(gel filtration chromatog. with; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 7429-90-5, Aluminum, biological studies 7439-89-6, Iron, biological studies 7439-91-0, Lanthanum, biological studies 7439-96-5, Manganese, biological studies 7439-98-7, Molybdenum, biological studies 7440-02-0, Nickel, biological studies 7440-22-4, Silver, biological studies 7440-24-6, Strontium, biological studies 7440-26-8, Technetium, biological studies 7440-33-7, Tungsten, biological studies 7440-38-2, Arsenic, biological studies 7440-39-3, Barium, biological studies 7440-43-9, Cadmium, biological studies 7440-50-8, Copper, biological studies 7440-57-5, Gold, biological studies 7440-58-6, Hafnium, biological studies 7440-66-6, Zinc, biological studies 7440-69-9, Bismuth, biological studies 7440-70-2, Calcium, biological studies 7782-49-2, Selenium, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(peptide domains contg.; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 9003-53-6D, Polystyrene, functionalized derivs.  
RL: NUU (Other use, unclassified); USES (Uses)  
(supports; synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 56-65-5, 5'-Atp, biological studies 70-18-8, Glutathione, biological studies 86-01-1, 5'-Gtp 97-77-8, Disulfiram  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 7440-48-4, Cobalt, biological studies  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)
- IT 76-05-1, Trifluoroacetic acid, uses  
RL: NUU (Other use, unclassified); USES (Uses)  
(synthetic and therapeutic methods for the alpha and beta domains of metallothionein)

RE.CNT 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD  
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L49 ANSWER 5 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:175791 HCAPLUS

DN 132:222549

TI Preparation of bis(piperazinyl) disulfides and analogs for treatment of papillomavirus-mediated disorders

IN Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui

PA Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.

SO PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07D203-24

ICS C07D205-04; C07D207-48; C07D209-48; C07D211-96; C07D213-76;  
 C07D239-28; C07D239-42; C07D243-08; C07D263-04; C07D265-30;  
 C07D295-194; C07D295-26; C07D317-58; C07C323-49; C07C333-32;  
 C07C381-00; A61K031-13; A61K031-145; A61K031-535

CC 28-17 (Heterocyclic Compounds (More Than One Hetero Atom))

Section cross-reference(s): 1

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000014063	A1	20000316	WO 1999-AU724	19990903
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	AU 9958401	A1	20000327	AU 1999-58401	19990903
	EP 1112250	A1	20010704	EP 1999-945758	19990903
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	JP 2002524442	T2	20020806	JP 2000-568822	19990903
PRAI	AU 1998-5733	A	19980904		
	AU 1999-1645	A	19990715		
	WO 1999-AU724	W	19990903		
OS	MARPAT 132:222549				
AB	R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoeq.2; n = 1-5], inhibitors of proteins encoded by an MPV gene by disruption of a chelated metal cation domain, were prep'd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prep'd. Data for biol. activity of I were given.				
ST	piperazinyl disulfide prepn treatment papillomavirus mediated disorder				
IT	Proteins, specific or class				
	RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)				
	(E6; prepn. of bis(piperazinyl) disulfides and analogs for treatment of				

**papillomavirus-mediated disorders)**

IT Transcription factors  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (E7; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

IT Uterus, neoplasm  
 Uterus, neoplasm  
 (cervix, inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

IT Antitumor agents  
 (cervix; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

IT Transforming proteins  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

IT Human papillomavirus 16  
 Human papillomavirus 18  
 Papillomavirus  
 (prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

IT 103-34-4P 729-46-4P 1623-84-3P  
 1623-85-4P 2759-28-6DP, N-Benzylpiperazine, 4,4'-polythiobis deriv. 6542-61-6P 7764-30-9P 10220-20-9P  
 15575-30-1P 26087-98-9P 35386-24-4DP,  
 1-(2-Methoxyphenyl)piperazine, 4,4'-polythiobis deriv. 36938-10-0P  
 59226-72-1P 85865-96-9P 98999-00-9P  
 260973-66-8P 260973-68-0P 260973-72-6P  
 260973-74-8P 260973-75-9P 260973-76-0P  
 260973-79-3P 260973-81-7P 260973-83-9P  
 260973-85-1P 260973-87-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus-mediated disorders)**

RE.CNT 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (1) Anon
- (2) Anon; Chromatographia 1989, 3-4, P113 HCAPLUS
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L49 ANSWER 6 OF 12 HCAPLUS COPYRIGHT 2002 ACS  
AN 1999:507293 HCAPLUS  
DN 132:87659  
TI Potential drugs against cervical cancer: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein  
AU **Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo;** Ganesan, Arasu; Rice, William G.; **Ting, Anthony E.**  
CS Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore  
SO Journal of the National Cancer Institute (1999), 91(14), 1211-1220  
CODEN: JNCIEQ; ISSN: 0027-8874  
PB Oxford University Press  
DT Journal  
LA English  
CC 1-1 (Pharmacology)  
Section cross-reference(s): 10  
AB The principal agent in the etiol. of cervical cancer, i.e., human **papillomavirus (HPV)** type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of **HPV** -contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic **HPV** -contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of **HPV**. These assay systems may be useful in the development of drugs against cervical cancer, genital warts, and asymptomatic infections by genital **HPVs**.  
ST assay **HPV** cervical cancer inhibitor design; human **papillomavirus** cervical cancer inhibitor assay; zinc binding oncoprotein **HPV** antitumor assay; redox reaction antiviral **HPV** design assay; p53 apoptosis cervical cancer inhibitor assay  
IT Proteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E5; potential drugs against cervical cancer)  
IT Proteins, specific or class  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E6; potential drugs against cervical cancer)  
IT Transcription factors  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E7; potential drugs against cervical cancer)  
IT Antiviral agents  
(anti- **HPV**; potential drugs against cervical cancer)  
IT Uterus, neoplasm  
Uterus, neoplasm  
(cervix, inhibitors; potential drugs against cervical cancer)

IT Antitumor agents  
(cervix; potential drugs against cervical cancer)

IT Analysis  
Apoptosis  
Drug design  
Drug screening  
Human papillomavirus  
Redox reaction  
(potential drugs against cervical cancer)

IT p53 (protein)  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(potential drugs against cervical cancer)

IT Fusion proteins (chimeric proteins)  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(potential drugs against cervical cancer)

IT 56-17-7, Cystamine dihydrochloride 56-89-3, Cystine, analysis 69-78-3  
97-77-8, Tetraethylthiuram disulfide 100-32-3 103-33-3,  
Azobenzene 103-34-4 119-80-2 120-78-5, 2,2'-  
Dithiobis(benzothiazole) 123-77-3, Azodicarbonamide 135-57-9,  
Bis(2-benzamidophenyl)disulfide 150-60-7, Dibenzyl disulfide 537-91-7,  
Bis(3-Nitrophenyl)disulfide 586-96-9, Nitrosobenzene 644-32-6, Benzoyl  
disulfide 870-93-9, DL-Homocystine 882-33-7, Phenyl disulfide  
940-69-2, .alpha.-Lipoamide 1141-88-4, 2,2'-Dithiodianiline 1155-00-6,  
Bis(2-nitrophenyl)disulfide 1160-68-5 2127-03-9, Aldrithiol 2  
5398-51-6 13895-38-0, 4-Nitrosoresorcinol-1-monomethyl ether  
15441-06-2, 3,3'-Dithiodipropionic acid dimethyl ester 16766-09-9,  
Bis(4-Acetamidophenyl)disulfide 26907-82-4 47231-30-1 108872-98-6  
120586-49-4, 1,2-Dithiane-4,5-diol, 1,1-dioxide, cis 207802-09-3  
RL: ANT (Analyte); ANST (Analytical study)  
(potential drugs against cervical cancer)

IT 7440-66-6, Zinc, biological studies 50812-37-8, Glutathione  
S-transferase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(potential drugs against cervical cancer)

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (51) Wright, T; Papillomavirus Rep 1994, V5, P175
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L49 ANSWER 7 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:196542 HCAPLUS

DN 124:223463

TI Carcinogenic and cocarcinogenic studies of thiram on mouse skin

AU Shukla, Y.; Baqar, S. M.; Mehrotra, N. K.

CS Industrial Toxicology Res. Centre, Mahatma Gandhi Marg, Lucknow, 226 001, India

SO Food Chem. Toxicol. (1996), 34(3), 283-9

CODEN: FCTOD7; ISSN: 0278-6915

DT Journal

LA English

CC 4-6 (Toxicology)

AB In the present study, the tumorigenic potential of thiram was evaluated in Swiss albino mice by a 2-stage initiation-promotion protocol and a long-term in vivo bioassay for carcinogenicity. Following tumor initiation with thiram and promotion with 12-O-tetradecanoylphorbol 13-acetate, skin tumors developed, mostly at the site of treatment (dorsal skin) in single and multiple dose-initiated animals. Similarly, **papillomatous** growths were obsd. on the dorsal skin of the mice initiated with a single subcarcinogenic dose of dimethylbenzanthracene and promoted with thiram. Thiram failed to provoke tumorigenesis when tested as a complete carcinogen for up to 52 wk and thereafter the study was terminated due to increased mortality. Thus, thiram has both tumor-initiating and tumor-promoting potential in both sexes of Swiss albino mice following topical exposure at the tested dose level.

ST skin tumor promotion thiram

IT Skin, neoplasm

(carcinogenic and cocarcinogenic studies of thiram on skin)

IT Carcinogens

(promoters, carcinogenic and cocarcinogenic studies of thiram on skin)

IT 137-26-8, Thiram

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(carcinogenic and cocarcinogenic studies of thiram on skin)

L49 ANSWER 8 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1988:563075 HCAPLUS

DN 109:163075

TI Effect of exogenous glutathione on tumor progression in the murine skin multistage carcinogenesis model

AU Rotstein, Joel B.; Slaga, Thomas J.

CS Cancer Cent., Univ. Texas Syst., Smithville, TX, 78957, USA

SO Carcinogenesis (London) (1988), 9(9), 1547-51

CODEN: CRNGDP; ISSN: 0143-3334

DT Journal

LA English

CC 1-6 (Pharmacology)

Section cross-reference(s): 4, 14

AB Oxidative stress has been suggested to play an integral role in the cancer process. It may be particularly significant during tumor progression, where there is likely to be a large amt. of free radicals generated by infiltrating inflammatory cells and dying tumor cells. In order to test this hypothesis, a variety of free radical scavengers and antioxidants were assessed for their ability to inhibit tumor progression. The murine skin multistage carcinogenesis model was used to generate **papillomas**, which are a population of putative precancerous lesions. Various test agents were applied topically to **papillomas** in order to det. if they would decrease the incidence of the malignant lesion, squamous cell carcinoma. The agents tested included: GSH, BHA, vitamin E, copper(II) (3,5-diisopropylsalicylate)2, sodium benzoate, N-acetyl cysteine and disulfiram. Under the conditions of the expts., only GSH and disulfiram inhibited tumor progression to a significant degree. Addnl. studies indicated that GSH prevented cancer development in a dose-dependent manner. Another expt. demonstrated that when **papillomas** received repeated topical applications of diethylmaleate, a GSH-depleting agent, tumor progression was enhanced. Collectively these data suggest that sufficient glutathione levels may be important in preventing cancer formation.

ST neoplasm oxidative stress antioxidant; free radical scavenger neoplasm; GSH tumor progress inhibition; disulfiram tumor progress inhibition

IT Neoplasm inhibitors

(antioxidants and free radical scavengers, disulfiram and DSH in relation to)

IT Radicals, biological studies

RL: BIOL (Biological study)

(scavengers, tumor progression inhibition response to)

IT Skin, neoplasm

(treatment of, with antioxidants and free radical scavengers, disulfiram and GSH in relation to)

IT Antioxidants

(tumor progression inhibition response to)

IT 59-02-9, D-.alpha.-Tocopherol 70-18-8, GSH, biological studies

97-77-8, Disulfiram 532-32-1, Sodium benzoate 616-91-1,

n-Acetylcysteine 21246-18-4 25013-16-5, BHA

RL: BIOL (Biological study)

(tumor progression inhibition response to)

L49 ANSWER 9 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1987:28723 HCAPLUS

DN 106:28723

TI Modifying effects of disulfiram on DNA adduct formation and persistence of benzaldehyde in N-nitroso-N-methylbenzylamine-induced carcinogenesis in rats

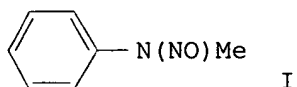
AU Schweinsberg, F.; Danecki, S.; Grotzke, J.; Von Karsa, L.; Buerkle, V.

CS Hygiene-Inst., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.

SO J. Cancer Res. Clin. Oncol. (1986), 112(2), 75-80

CODEN: JCROD7; ISSN: 0171-5216

DT Journal  
 LA English  
 CC 4-6 (Toxicology)  
 Section cross-reference(s): 1  
 GI



- AB The effects were studied of disulfiram (DSF) [97-77-8] on long-term application of N-nitroso-N-methylbenzylamine (NMBA) (I) [937-40-6]. HPLC and fluorescence detection were used to det. O6-methylguanine (O6-MG) [20535-83-5] in DNA obtained from the respiratory tract of rats subjected to long-term simultaneous application of DSF and NMBA. After 2 days of treatment, more O6-MG was detected in the proximal portion of the respiratory tract, including the trachea and main bronchi, than in the distal portion. The findings were reversed after 10 and 30 days, at which time formation of the DNA adduct was substantially higher in the distal portion of the respiratory tract, despite increases in both portions. The biochem. results corresponded to morphol. findings. Initially, increased nos. of metabolizing goblet cells appeared in mucous cell hyperplasia in the proximal respiratory tract. Subsequently, the hyperplasia migrated to distal regions of the respiratory tract; at this stage, the goblet cells disappeared from the proximal portion, which now revealed toxic degeneration, atrophy, and subsequent squamous metaplasia of the mucous lining and squamous **papillomas**. At various times during a 40-day period, 2-7-fold more O6-MG in pulmonary DNA was detected in rats treated with DSF and NMBA than with NMBA alone, whereby distinct amts. of O6-MG were found in the latter animals. In contrast to the above-mentioned morphol. findings, no morphol. alterations occurred in the respiratory tract of the animals treated with NMBA alone. It is therefore conceivable that the above pathol. lesions resulted not merely from the presence of DNA adducts, but also from an addnl., previously unspecified effect. As benzaldehyde (BA) [100-52-7] is formed in equimolar amts. in NMBA metab. and DSF has been demonstrated to inhibit aldehyde metab., this aldehyde is a possible candidate for such an effect. In the present study, rats were therefore treated with BA, DSF, or NMBA, or combinations thereof. Long-term application of BA alone led to goblet cell hyperplasia, hyperplasia of the peribronchial lymphatic system, mucous epithelial atrophy, and accompanying perivascularitis - the same alterations seen under long-term application of NMBA and DSF. The changes were most pronounced in the group with concomitant application of NMBA, DSF, and BA. Apparently, BA plays a role in pathol. changes obsd. under the influence of NMBA.
- ST disulfiram DNA benzaldehyde nitrosomethylbenzylamine carcinogenesis  
 IT Neoplasm  
     **Papilloma**  
       (from nitrosomethylbenzylamine, of respiratory tract, disulfiram effect on, mechanism of)
- IT Deoxyribonucleic acids  
 RL: BIOL (Biological study)  
     (nitrosomethylbenzylamine adducts, of lung, disulfiram effect on, lung neoplasm in relation to)
- IT Respiratory tract  
     (disease, metaplasia, from nitrosomethylbenzylamine, disulfiram effect on, mechanism of)
- IT Respiratory tract  
     (neoplasm, from nitrosomethylbenzylamine, disulfiram effect on, mechanism of)

IT 100-52-7, Benzaldehyde, biological studies  
RL: FORM (Formation, nonpreparative)  
(formation of, from nitrosomethylbenzylamine, in lung, lung neoplasm in relation to)

IT 937-40-6, N-Nitroso-N-methylbenzylamine  
RL: BIOL (Biological study)  
(lung neoplasm induction by, disulfiram effect on, benzaldehyde in relation to)

IT 97-77-8, Disulfiram  
RL: BIOL (Biological study)  
(nitrosomethylbenzylamine-induced lung neoplasm response to, benzaldehyde in relation to)

IT 20535-83-5  
RL: BIOL (Biological study)  
(of lung DNA, in nitrosomethylbenzylamine-induced lung neoplasm)

L49 ANSWER 10 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1985:466487 HCAPLUS

DN 103:66487

TI Role of the respiratory system in metabolism of N-nitrosamines after simultaneous application of disulfiram

AU Buerkle, V.; Wittenberg, H.; Schweinsberg, F.; Weissenberger, I.; Schweinsberg, E.; Brueckner, B.

CS Pathol. Inst., Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.

SO IARC Sci. Publ. (1984), 57(N-Nitroso Compd: Occurrence, Biol. Eff. Relevance Hum. Cancer), 533-41  
CODEN: IARCCD; ISSN: 0300-5038

DT Journal

LA English

CC 4-6 (Toxicology)

AB Subsequent to modification of N-nitrosamines metab. by disulfiram [97-77-8], mucus-producing cells and Clara cells in the respiratory tract are involved increasingly in detoxification as well as in bioactivation of N-nitroso-N-methylbenzylamine [937-40-6] and N-nitrosodibutylamine [924-16-3]. Overtaxing of these cells or local concn. of antigenic metabolites leads to cytolytic defects in tracheal, bronchial, and bronchiolar epithelium, in addn. to toxic degenerative lesions. The resulting continuous stimulation of proliferation leads to basal-cell hyperplasia, squamous-cell metaplasia, and squamous **papillomas**. In areas with insufficient differentiation, due to cell proliferation, there is an increased probability that focal mutation, subsequent to alkylation of purine bases, will be passed from 1 cell generation to the next, with subsequent formation of tumors in the bronchioloalveolar region.

ST nitrosamine metab disulfiram neoplasm

IT Neoplasm

(from nitrosamine, of respiratory tract, disulfiram effect on)

IT Respiratory tract

(neoplasm, from nitrosamine, disulfiram effect on)

IT 924-16-3 937-40-6

RL: BIOL (Biological study)

(neoplasm from, of respiratory tract, disulfiram effect on)

IT 97-77-8

RL: BIOL (Biological study)

(nitrosamine metab. response to, respiratory tract neoplasm in relation to)

L49 ANSWER 11 OF 12 HCAPLUS COPYRIGHT 2002 ACS

AN 1984:585821 HCAPLUS

DN 101:185821

TI Induction of tumors of the nasal cavity in rats by concurrent feeding of thiram and sodium nitrite

AU Lijinsky, William



CS Chem. Carcinog. Lab., Natl. Cancer Inst., Frederick, MD, 21701, USA  
SO J. Toxicol. Environ. Health (1984), 13(4-6), 609-14  
CODEN: JTEHD6; ISSN: 0098-4108  
DT Journal  
LA English  
CC 4-6 (Toxicology)  
AB Simultaneous feeding to rats of thiram [137-26-8] with NaNO<sub>2</sub> was carried out to assess the possibility of formation of carcinogenic N-nitroso derivs. in vivo. Following the administration of feed contg. 500 ppm thiram plus 2000 ppm NaNO<sub>2</sub> for 104 wk, a high incidence of tumors of the nasal cavity was found in both sexes, 18 of 24 males and 15 of 24 females. No nasal cavity tumors were seen in untreated rats, or those given 500 ppm of thiram or 2000 ppm of NaNO<sub>2</sub> alone. A 20% incidence of **papillomas** of the forestomach was also seen in the rats of both sexes given the combined treatment. The other significant difference in incidence of tumors between the rats given thiram with or without nitrite was a decreased no. of animals with monocytic leukemia, which is a common neoplasm in untreated F344 rats.  
ST nose neoplasm thiram nitrite  
IT **Papilloma**  
(from sodium nitrite and thiram, of forestomach)  
IT Neoplasm  
(from sodium nitrite and thiram, of nasal cavity)  
IT Nose  
(neoplasm, from sodium nitrite and thiram)  
IT **137-26-8**  
RL: BIOL (Biological study)  
(nasal cavity tumor induction by sodium nitrite and)  
IT 7632-00-0  
RL: BIOL (Biological study)  
(nasal cavity tumor induction by thiram and)

L49 ANSWER 12 OF 12 HCAPLUS COPYRIGHT 2002 ACS  
AN 1982:47372 HCAPLUS  
DN 96:47372  
TI Effect of disulfiram on the toxicity and carcinogenicity of N-methyl-N-nitrosobenzylamine in rats  
AU Schweinsberg, F; Buerkle, V.  
CS Hyg. Inst., Univ. Tuebingen, Tuebingen, D-7400, Fed. Rep. Ger.  
SO J. Cancer Res. Clin. Oncol. (1981), 102(1), 43-7  
CODEN: JCROD7; ISSN: 0171-5216  
DT Journal  
LA German  
CC 4-6 (Toxicology)  
AB The simultaneous administration of 200 or 710 mg/kg diet of disulfiram [97-77-8] to female SIV 50 rats receiving 10 mg/L N-methyl-N-nitrosobenzylamine [937-40-6] in drinking water increased the toxicity of the latter markedly and accelerated the formation of esophageal tumors. Tracheal squamous cell **papillomas** and potentially precancerous squamous cell metaplasia in the bronchial system were found also.  
ST methylnitrosobenzylamine carcinogenicity toxicity disulfiram; benzylamine methylnitroso carcinogenicity toxicity disulfiram  
IT Neoplasm  
(from methylnitrosobenzylamine, disulfiram effect on)  
IT Esophagus  
Trachea  
(neoplasm, from methylnitrosobenzylamine, disulfiram effect on)  
IT Bronchi  
(neoplasms, from methylnitrosobenzylamine, disulfiram effect on)  
IT 937-40-6  
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)  
(carcinogenicity and toxicity of, disulfiram effect on)

IT 97-77-8

RL: BIOL (Biological study)  
(methylnitrosobenzylamine carcinogenicity and toxicity response to)

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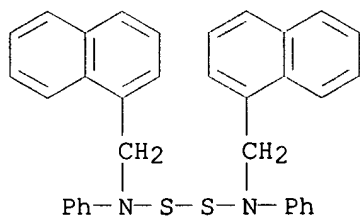
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for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L50 ANSWER 1 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 320609-22-1 REGISTRY  
CN 1-Naphthalenemethanamine, N,N'-dithiobis[N-phenyl- (9CI) (CA INDEX NAME)  
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SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



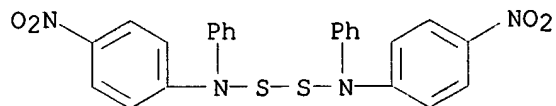
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REFERENCE 1: 134:110110

L50 ANSWER 2 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 320609-21-0 REGISTRY  
CN Benzenamine, N,N'-dithiobis[4-nitro-N-phenyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H18 N4 O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

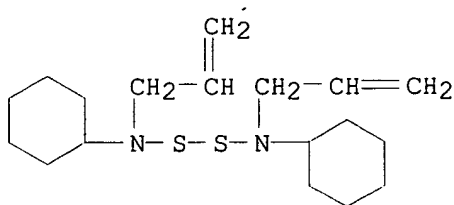


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1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 3 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-19-6** REGISTRY  
CN Cyclohexanamine, N,N'-dithiobis[N-2-propenyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C18 H32 N2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

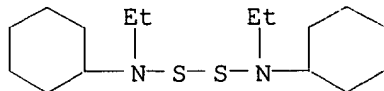


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 4 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-18-5** REGISTRY  
CN Cyclohexanamine, N,N'-dithiobis[N-ethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C16 H32 N2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

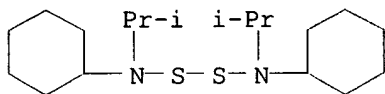


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 5 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN **320609-17-4** REGISTRY  
 CN Cyclohexanamine, N,N'-dithiobis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C18 H36 N2 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

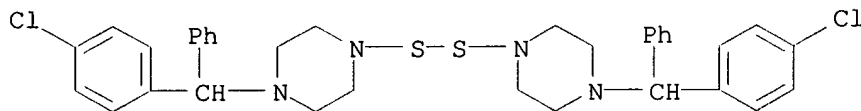


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 6 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN **320609-16-3** REGISTRY  
 CN Piperazine, 1,1'-dithiobis[4-[(4-chlorophenyl)phenylmethyl]- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C34 H36 Cl2 N4 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

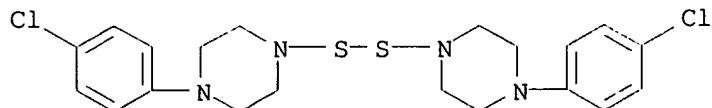


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 7 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN **320609-15-2** REGISTRY  
 CN Piperazine, 1,1'-dithiobis[4-(4-chlorophenyl)- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C20 H24 Cl2 N4 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

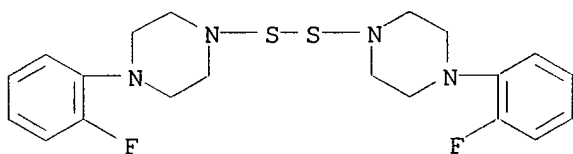


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 8 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-14-1** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(2-fluorophenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H24 F2 N4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

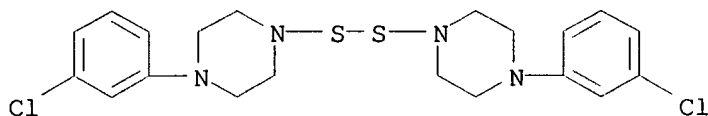


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 9 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-13-0** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(3-chlorophenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H24 Cl2 N4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

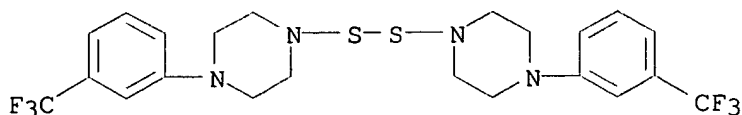


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 10 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-12-9** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-[3-(trifluoromethyl)phenyl]- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H24 F6 N4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

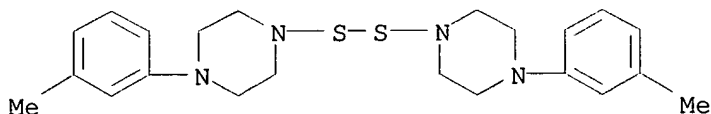


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 11 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-11-8** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(3-methylphenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H30 N4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

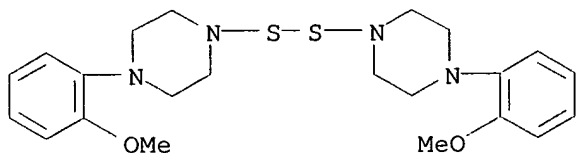


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 12 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-10-7** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(2-methoxyphenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H30 N4 O2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

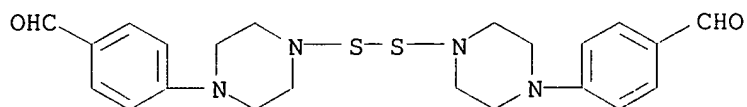


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 13 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-09-4** REGISTRY  
CN Benzaldehyde, 4,4'-(dithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H26 N4 O2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

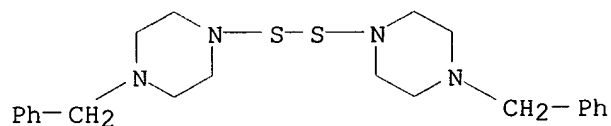


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 14 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-08-3** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(phenylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H30 N4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

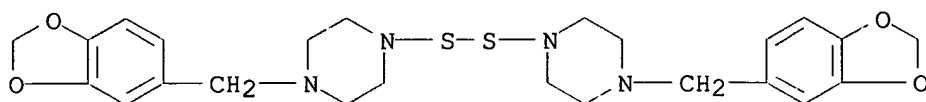


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 15 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **320609-07-2** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H30 N4 O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

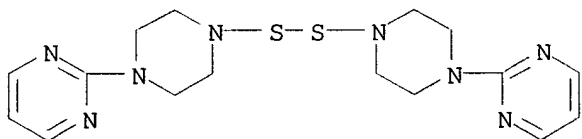


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 16 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 320609-06-1 REGISTRY  
CN Pyrimidine, 2,2'-(dithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C16 H22 N8 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

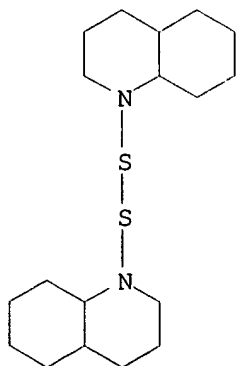


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 17 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 320609-05-0 REGISTRY  
CN Quinoline, 1,1'-dithiobis[decahydro- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C18 H32 N2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



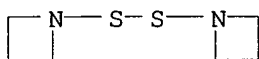


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 18 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 320609-04-9 REGISTRY  
 CN Azetidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C6 H12 N2 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

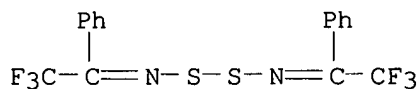


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 19 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 303796-55-6 REGISTRY  
 CN Benzenemethanimine, N,N'-dithiobis[.alpha.-(trifluoromethyl)- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C16 H10 F6 N2 S2  
 SR Chemical Library  
 LC STN Files: CA, CAPLUS, CHEMCATS, TOXCENTER

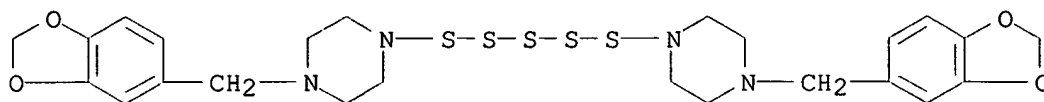


## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

L50 ANSWER 20 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 260973-87-3 REGISTRY  
 CN Piperazine, 1,1'-pentathio-bis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C24 H30 N4 O4 S5  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

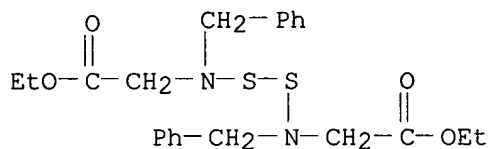


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 21 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 260973-85-1 REGISTRY  
CN Glycine, N,N'-dithiobis[N-(phenylmethyl)-, diethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H28 N2 O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



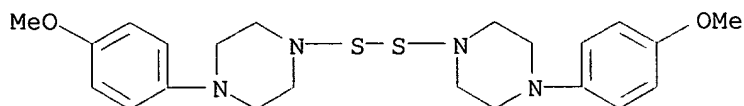
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 22 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 260973-83-9 REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(4-methoxyphenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C22 H30 N4 O2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



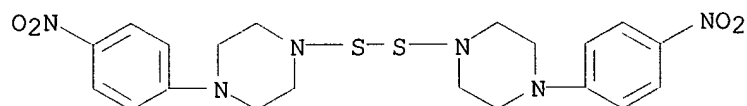
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 23 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **260973-81-7** REGISTRY  
CN Piperazine, 1,1'-dithiobis[4-(4-nitrophenyl)- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C20 H24 N6 O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



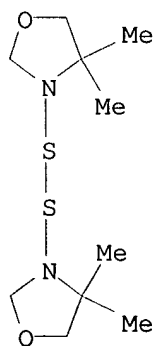
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 24 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **260973-79-3** REGISTRY  
CN Oxazolidine, 3,3'-dithiobis[4,4-dimethyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C10 H20 N2 O2 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

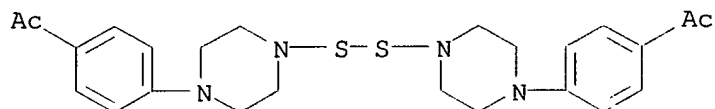
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 25 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 260973-76-0 REGISTRY  
 CN Ethanone, 1,1'-[dithiobis(4,1-piperazinediyl-4,1-phenylene)]bis- (9CI)  
 (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C24 H30 N4 O2 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER



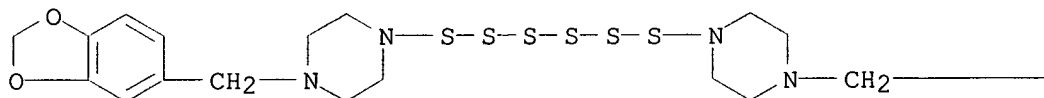
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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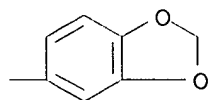
REFERENCE 1: 132:222549

L50 ANSWER 26 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 260973-75-9 REGISTRY  
 CN Piperazine, 1,1'-hexathiobis[4-(1,3-benzodioxol-5-ylmethyl)- (9CI) (CA  
 INDEX NAME)  
 FS 3D CONCORD  
 MF C24 H30 N4 O4 S6  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

PAGE 1-A



PAGE 1-B

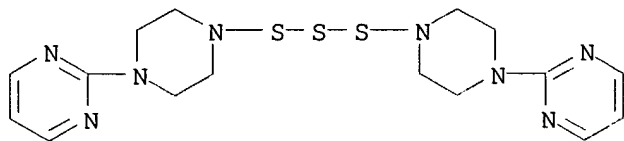


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 27 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 260973-74-8 REGISTRY  
 CN Pyrimidine, 2,2'-(trithiodi-4,1-piperazinediyl)bis- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C16 H22 N8 S3  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER

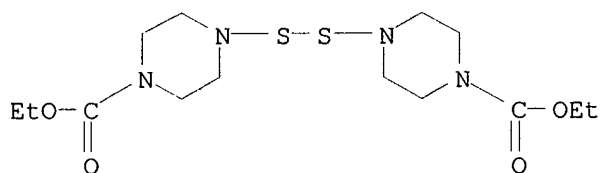


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 28 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **260973-72-6** REGISTRY  
CN 1-Piperazinecarboxylic acid, 4,4'-dithiobis-, diethyl ester (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C14 H26 N4 O4 S2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER



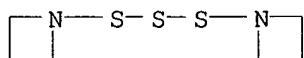
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 29 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **260973-68-0** REGISTRY  
CN Azetidine, 1,1'-trithiobis- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C6 H12 N2 S3  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER

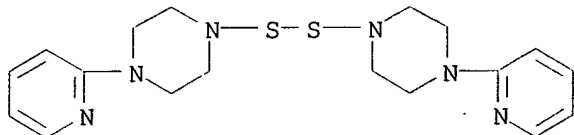


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 132:222549

L50 ANSWER 30 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 260973-66-8 REGISTRY  
 CN Piperazine, 1,1'-dithiobis[4-(2-pyridinyl)- (9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C18 H24 N6 S2  
 SR CA  
 LC STN Files: CA, CAPLUS, TOXCENTER



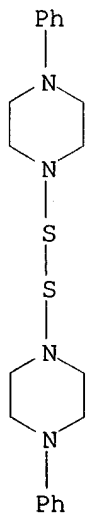
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 31 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 103388-17-6 REGISTRY  
 CN Piperazine, 1,1'-dithiobis[4-phenyl- (6CI, 9CI) (CA INDEX NAME)  
 FS 3D CONCORD  
 MF C20 H26 N4 S2  
 SR CAOLD  
 LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, TOXCENTER  
 (\*File contains numerically searchable property data)



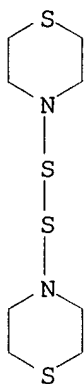
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

L50 ANSWER 32 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **98999-00-9** REGISTRY  
CN Thiomorpholine, 4,4'-dithiobis- (6CI, 9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C8 H16 N2 S4  
SR CAOLD  
LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER



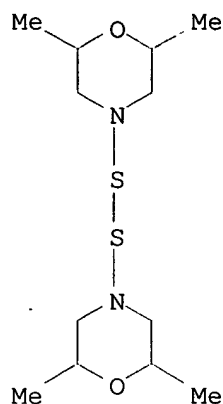
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

L50 ANSWER 33 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN **85865-96-9** REGISTRY  
CN Morpholine, 4,4'-dithiobis[2,6-dimethyl- (6CI, 9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C12 H24 N2 O2 S2  
SR Commission of European Communities  
LC STN Files: CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMLIST, TOXCENTER,  
USPATFULL  
Other Sources: EINECS\*\*  
(\*Enter CHEMLIST File for up-to-date regulatory information)



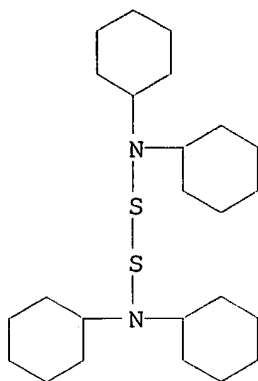
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8 REFERENCES IN FILE CA (1967 TO DATE)  
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8 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110  
REFERENCE 2: 132:222549  
REFERENCE 3: 123:345471  
REFERENCE 4: 114:41666  
REFERENCE 5: 112:181185  
REFERENCE 6: 112:58046  
REFERENCE 7: 112:37910  
REFERENCE 8: 111:98806

L50 ANSWER 34 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 72896-38-9 REGISTRY  
CN Cyclohexanamine, N,N'-dithiobis[N-cyclohexyl- (9CI) (CA INDEX NAME)  
FS 3D CONCORD  
MF C24 H44 N2 S2  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 99:25267

REFERENCE 3: 92:119716

L50 ANSWER 35 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 62158-06-9 REGISTRY

CN Benzenemethanamine, N,N'-dithiobis[N-(1-methylethyl)- (9CI) (CA INDEX NAME)

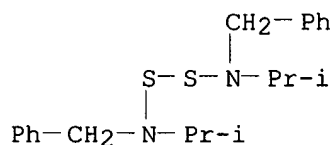
OTHER NAMES:

CN N,N'-Dithiobis[N-isopropylbenzylamine]

FS 3D CONCORD

MF C20 H28 N2 S2

LC STN Files: BEILSTEIN\*, CA, CAPLUS, TOXCENTER  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 86:120244

L50 ANSWER 36 OF 50 REGISTRY COPYRIGHT 2002 ACS

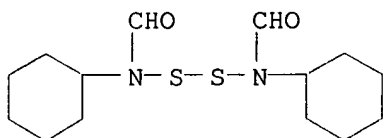
RN 59226-72-1 REGISTRY

CN Formamide, N,N'-dithiobis[N-cyclohexyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C14 H24 N2 O2 S2

LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB, TOXCENTER,  
USPATFULL  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

4 REFERENCES IN FILE CA (1967 TO DATE)  
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 86:120883

REFERENCE 4: 84:179730

L50 ANSWER 37 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN **36938-10-0** REGISTRY

CN Piperazine, 1,1'-dithiobis[4-methyl- (6CI, 7CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1,1'-Dithiobis[4-methylpiperazine]

CN Bis(4-methyl-1-piperazinyl) disulfide

CN Dithiobis[N-methylpiperazine]

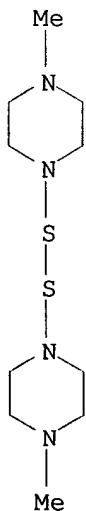
FS 3D CONCORD

MF C10 H22 N4 S2

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS, RTECS\*,  
TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)



**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

10 REFERENCES IN FILE CA (1967 TO DATE)  
10 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110  
REFERENCE 2: 132:222549  
REFERENCE 3: 127:347482  
REFERENCE 4: 122:316653  
REFERENCE 5: 122:108352  
REFERENCE 6: 119:51087  
REFERENCE 7: 105:171948  
REFERENCE 8: 99:25267  
REFERENCE 9: 80:37060  
REFERENCE 10: 77:63107

L50 ANSWER 38 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN **26087-98-9** REGISTRY

CN 1H-1,4-Diazepine, 1,1'-(dithiodicarbonothioyl)bis[hexahydro-4-methyl-  
(9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Disulfide, bis[(hexahydro-4-methyl-1H-1,4-diazepin-1-yl)thiocarbonyl]  
(8CI)

OTHER NAMES:

CN Bis(4-methyl-1-homopiperazinylthiocarbonyl) disulfide

CN FLA 63

FS 3D CONCORD

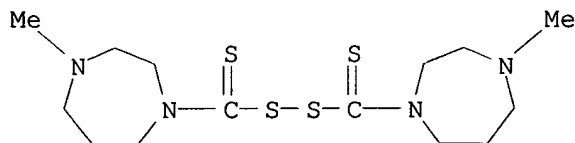
MF C14 H26 N4 S4

LC STN Files: BEILSTEIN\*, BIOSIS, BIOTECHNO, CA, CAPLUS, CHEMCATS,  
CHEMLIST, CSCHEM, DDFU, DRUGU, EMBASE, IFICDB, IFIPAT, IFIUDB, MEDLINE,  
PHAR, PROMT, RTECS\*, TOXCENTER, USPATFULL

(\*File contains numerically searchable property data)

Other Sources: EINECS\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)

**\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\***

109 REFERENCES IN FILE CA (1967 TO DATE)  
109 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:110110  
REFERENCE 2: 132:222549

REFERENCE 3: 125:127644  
 REFERENCE 4: 119:20007  
 REFERENCE 5: 118:188689  
 REFERENCE 6: 115:174663  
 REFERENCE 7: 115:106556  
 REFERENCE 8: 114:178040  
 REFERENCE 9: 107:52640  
 REFERENCE 10: 107:664

L50 ANSWER 39 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 16131-50-3 REGISTRY

CN Benzenemethanamine, N,N'-dithiobis[N-(phenylmethyl)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Dibenzylamine, N,N'-dithiobis- (6CI, 8CI)

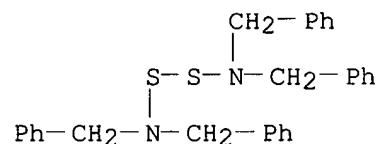
OTHER NAMES:

CN Dithiobis(dibenzylamine)

CN N,N'-Dithiobis(dibenzylamine)

MF C28 H28 N2 S2

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

9 REFERENCES IN FILE CA (1967 TO DATE)  
 9 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110  
 REFERENCE 2: 127:347482  
 REFERENCE 3: 125:302994  
 REFERENCE 4: 122:316653  
 REFERENCE 5: 116:20620  
 REFERENCE 6: 115:231541  
 REFERENCE 7: 115:221795  
 REFERENCE 8: 112:178823  
 REFERENCE 9: 111:146042

L50 ANSWER 40 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 15575-30-1 REGISTRY  
CN Ethanamine, N,N'-dithiobis[N-ethyl- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Diethylamine, N,N'-dithiobis- (7CI, 8CI)  
OTHER NAMES:  
CN Bis(diethylamino) disulfide  
CN Dithiobis[diethylamine]  
CN N,N'-Dithiobis(diethylamine)  
FS 3D CONCORD  
DR 98543-47-6  
MF C8 H20 N2 S2  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, CHEMINFORMRX,  
DETERM\*, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

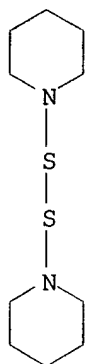
Et<sub>2</sub>N-S-S-NEt<sub>2</sub>

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

23 REFERENCES IN FILE CA (1967 TO DATE)  
23 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:262761  
REFERENCE 2: 134:110110  
REFERENCE 3: 132:222549  
REFERENCE 4: 116:20620  
REFERENCE 5: 115:221795  
REFERENCE 6: 115:182227  
REFERENCE 7: 112:178823  
REFERENCE 8: 107:217421  
REFERENCE 9: 97:39023  
REFERENCE 10: 94:183348

L50 ANSWER 41 OF 50 REGISTRY COPYRIGHT 2002 ACS  
RN 10220-20-9 REGISTRY  
CN Piperidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Piperidine, 1,1'-dithiodi- (6CI, 7CI, 8CI)  
OTHER NAMES:  
CN 1,1'-Dithiodipiperidine  
CN Dipiperidino disulfide  
CN N,N'-Dithiobis(piperidine)  
FS 3D CONCORD  
MF C10 H20 N2 S2  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,  
CHEMINFORMRX, CSCHEM, GMELIN\*, HODOC\*, IFICDB, IFIPAT, IFIUDB, RTECS\*,  
SPECINFO, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

49 REFERENCES IN FILE CA (1967 TO DATE)  
49 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
14 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:73255  
REFERENCE 2: 134:110110  
REFERENCE 3: 132:222549  
REFERENCE 4: 126:143785  
REFERENCE 5: 126:18633  
REFERENCE 6: 120:164086  
REFERENCE 7: 116:20620  
REFERENCE 8: 115:231541  
REFERENCE 9: 115:221795  
REFERENCE 10: 113:211924

L50 ANSWER 42 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 7764-30-9 REGISTRY

CN 1H-Isoindole-1,3(2H)-dione, 2,2'-dithiobis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Phthalimide, N,N'-dithiodi- (7CI)

OTHER NAMES:

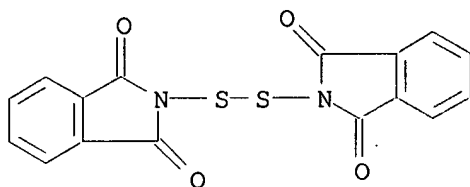
CN N,N'-Dithiobis(phthalimide)

FS 3D CONCORD

MF C16 H8 N2 O4 S2

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,  
CHEMINFORMRX, GMELIN\*, IFICDB, IFIPAT, IFIUDB, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

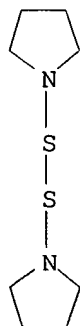


\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

26 REFERENCES IN FILE CA (1967 TO DATE)  
 26 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:70673  
 REFERENCE 2: 135:53776  
 REFERENCE 3: 134:110110  
 REFERENCE 4: 132:222549  
 REFERENCE 5: 127:66018  
 REFERENCE 6: 123:112220  
 REFERENCE 7: 115:255749  
 REFERENCE 8: 114:206663  
 REFERENCE 9: 109:242969  
 REFERENCE 10: 109:54039

L50 ANSWER 43 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 6542-61-6 REGISTRY  
 CN Pyrrolidine, 1,1'-dithiobis- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Pyrrolidine, 1,1'-dithiodi- (7CI, 8CI)  
 OTHER NAMES:  
 CN 1-Pyrrolidinyl disulfide  
 FS 3D CONCORD  
 MF C8 H16 N2 S2  
 CI COM  
 LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER



## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6 REFERENCES IN FILE CA (1967 TO DATE)  
6 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 117:183804

REFERENCE 4: 114:41666

REFERENCE 5: 94:183348

REFERENCE 6: 84:89215

L50 ANSWER 44 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 2129-27-3 REGISTRY

CN Benzenamine, N,N'-dithiobis[N-phenyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Diphenylamine, N,N'-dithiobis- (7CI)

OTHER NAMES:

CN Bis(diphenylamino) disulfide

FS 3D CONCORD

MF C24 H20 N2 S2

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)Ph2N-S-S-NPh2

## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5 REFERENCES IN FILE CA (1967 TO DATE)  
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 94:183348

REFERENCE 3: 92:119716

REFERENCE 4: 89:107376

REFERENCE 5: 84:89215

L50 ANSWER 45 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 1623-85-4 REGISTRY

CN Aziridine, 1,1'-dithiobis[2-methyl- (7CI, 8CI, 9CI) (CA INDEX NAME)

OTHER NAMES:

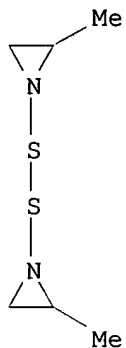
CN ENT 50361

FS 3D CONCORD

MF C6 H12 N2 S2

LC STN Files: CA, CAOLD, CAPLUS, TOXCENTER





\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
 3 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 4 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 70:10608

L50 ANSWER 46 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN **1623-84-3** REGISTRY

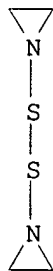
CN Aziridine, 1,1'-dithiobis- (7CI, 8CI, 9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C4 H8 N2 S2

CI COM

LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, TOXCENTER  
 (\*File contains numerically searchable property data)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

6 REFERENCES IN FILE CA (1967 TO DATE)  
 6 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 8 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 134:110110

REFERENCE 2: 132:222549

REFERENCE 3: 115:122307

REFERENCE 4: 70:10608

REFERENCE 5: 69:35917

REFERENCE 6: 67:90726

L50 ANSWER 47 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN **729-46-4** REGISTRY

CN Morpholine, 4,4'-(dithiodicarbonothioyl)bis- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Disulfide, bis(morpholinethiocarbonyl) (6CI, 7CI, 8CI)

OTHER NAMES:

CN 4-Morpholinethiocarbonyl disulfide

CN Bis(4-morpholinethiocarbonyl) disulfide

CN Bis(morpholinethiocarbonyl) disulfide

CN Dimorpholinethiuram disulfide

CN Disulfide, bis(4-morpholinylthioxomethyl)

CN NSC 402538

CN Thiuram disulfide, bis(oxydi-2,1-ethanediyl)-

FS 3D CONCORD

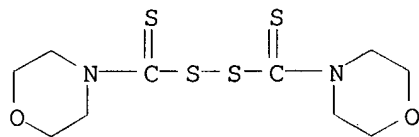
MF C10 H16 N2 O2 S4

LC STN Files: BEILSTEIN\*, BIOSIS, CA, CAOLD, CAPLUS, CASREACT, CHEMCATS,  
CHEMLIST, GMELIN\*, IFICDB, IFIPAT, IFIUDB, RTECS\*, SPECINFO, TOXCENTER,  
USPATFULL

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

63 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

63 REFERENCES IN FILE CAPLUS (1967 TO DATE)

18 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:184061

REFERENCE 2: 134:237436

REFERENCE 3: 134:110110

REFERENCE 4: 133:222350

REFERENCE 5: 132:222549

REFERENCE 6: 132:59191

REFERENCE 7: 129:92767

REFERENCE 8: 125:184901

REFERENCE 9: 124:29364

REFERENCE 10: 122:186597

L50 ANSWER 48 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 137-26-8 REGISTRY

CN Thioperoxydicarbonic diamide ([H2N)C(S)]2S2), tetramethyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Disulfide, bis(dimethylthiocarbamoyl) (8CI)

OTHER NAMES:

CN AApirol

CN Aatiram

CN Accel TMT

CN Accelerant T

CN Accelerator T

CN Accelerator Thiuram

CN Aceto TETD

CN Anles

CN Arasan

CN Arasan 42S

CN Arasan 50 red

CN Arasan 70

CN Arasan 70-S Red

CN Arasan 75

CN Arasan M

CN Arasan-SF

CN Atiram

CN Basultra

CN Betoxin

CN Bis(dimethylthiocarbamoyl) disulfide

CN Bis(dimethylthiocarbamyl) disulfide

CN Cunitex

CN Delsan

CN Ekagom TB

CN Emol

CN Falitiram

CN Ferna-Col

CN Fernasan

CN Fernasan A

CN Fernide

CN Formalsol

CN Hermal

CN Hermat TMT

CN Heryl

CN Hexathir

CN Kregasan

CN Mercuram

CN Methyl Thiram

CN Methyl Tuads

CN Metiur

CN Metiurac

CN N,N,N',N'-Tetramethylthiuram disulfide

CN Nobecutan

CN Nocceler TT

CN Normersan

CN NSC 1771

CN Orac TMTD

CN Panoram 75

CN Perkacit TMTD

ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY

FS 3D CONCORD

DR 12680-07-8, 12680-62-5, 56645-31-9, 66173-72-6, 93196-73-7, 39456-80-9

MF C6 H12 N2 S4

CI COM

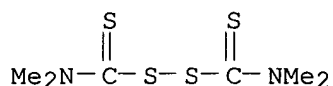
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,

BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
 CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU,  
 DIOGENES, DRUGU, EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIADB,  
 IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHARMASEARCH, PIRA, PROMT,  
 RTECS\*, SPECINFO, SYNTHLINE, TOXCENTER, ULIDAT, USAN, USPAT2, USPATFULL,  
 VETU

(\*File contains numerically searchable property data)

Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*, WHO

(\*\*Enter CHEMLIST File for up-to-date regulatory information)



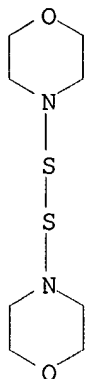
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

5345 REFERENCES IN FILE CA (1967 TO DATE)  
 90 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 5347 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 51 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:83098  
 REFERENCE 2: 137:80050  
 REFERENCE 3: 137:74595  
 REFERENCE 4: 137:64352  
 REFERENCE 5: 137:59004  
 REFERENCE 6: 137:47787  
 REFERENCE 7: 137:35457  
 REFERENCE 8: 137:34375  
 REFERENCE 9: 137:34370  
 REFERENCE 10: 137:16590

L50 ANSWER 49 OF 50 REGISTRY COPYRIGHT 2002 ACS  
 RN 103-34-4 REGISTRY  
 CN Morpholine, 4,4'-dithiobis- (9CI) (CA INDEX NAME)  
 OTHER CA INDEX NAMES:  
 CN Morpholine, 4,4'-dithiodi- (6CI, 7CI, 8CI)  
 OTHER NAMES:  
 CN 4,4'-Dithiobis[morpholine]  
 CN 4,4'-Dithiodimorpholine  
 CN Accel R  
 CN Bismorpholine disulfide  
 CN Bismorpholino disulfide  
 CN Deovulc M  
 CN Di(4-morpholinyl) disulfide  
 CN DTDM  
 CN Morpholine disulfide  
 CN Morpholinodisulfide  
 CN N,N'-Bismorpholine disulfide  
 CN N,N'-Dimorpholinyl disulfide  
 CN N,N'-Dithiobis[morpholine]

CN N,N'-Dithiodimorpholine  
 CN Rhenocure M/G  
 CN Sanfel R  
 CN Sulfasan  
 CN Sulfasan DTDM  
 CN Sulfasan R  
 CN Vanax A  
 CN Vulnoc R  
 FS 3D CONCORD  
 DR 39393-19-6  
 MF C8 H16 N2 O2 S2  
 CI COM  
 LC STN Files: BEILSTEIN\*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CANCERLIT,  
 CAOLD, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CHEMLIST, CIN, CSCHEM,  
 CSNB, EMBASE, HODOC\*, HSDB\*, IFICDB, IFIPAT, IFIUDB, MEDLINE, MRCK\*,  
 MSDS-OHS, NIOSHTIC, PROMT, RTECS\*, TOXCENTER, USPATFULL  
 (\*File contains numerically searchable property data)  
 Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

502 REFERENCES IN FILE CA (1967 TO DATE)  
 5 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
 503 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
 42 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:73255  
 REFERENCE 2: 137:35409  
 REFERENCE 3: 137:34375  
 REFERENCE 4: 137:34370  
 REFERENCE 5: 136:388294  
 REFERENCE 6: 136:341988  
 REFERENCE 7: 136:329488  
 REFERENCE 8: 136:329305  
 REFERENCE 9: 136:327942

REFERENCE 10: 136:262761

L50 ANSWER 50 OF 50 REGISTRY COPYRIGHT 2002 ACS

RN 97-77-8 REGISTRY

CN Thioperoxydicarbonic diamide ( $[(H_2N)C(S)]_2S_2$ ), tetraethyl- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN Disulfide, bis(diethylthiocarbamoyl) (8CI)

OTHER NAMES:

CN Abstensil

CN Abstinil

CN Abstiny

CN Accel TET

CN Accel TET-R

CN Alcophobin

CN Antabus

CN Antabuse

CN Antadix

CN Antaethyl

CN Antalcol

CN Antetan

CN Antetil

CN Anticol

CN Antietanol

CN Antietil

CN Antikol

CN Antivitium

CN Aversan

CN Averzan

CN Bis(diethylthiocarbamoyl) disulfide

CN Bis(N,N-diethylthiocarbamoyl) disulfide

CN Contralin

CN Cronetal

CN Dicupral

CN Disulfiram

CN Ekagom DTET

CN Ekagom TEDS

CN Ekagom TETDS

CN Espenal

CN Esperal

CN Etabus

CN Ethyl Thiram

CN Ethyl Thiurad

CN Ethyl Tuads

CN Ethyl Tuex

CN Exhorran

CN Hoca

CN Krotenal

CN N,N,N',N'-Tetraethylthiuram disulfide

CN Nocceler TET

CN Nocceler TET-G

CN Noxal

CN NSC 25953

CN Refusal

CN Sanceler TET

CN Sanceler TET-G

CN Soxinol TET

CN Stopetyl

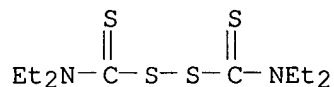
ADDITIONAL NAMES NOT AVAILABLE IN THIS FORMAT - Use FCN, FIDE, or ALL for DISPLAY

FS 3D CONCORD

DR 11078-22-1, 155-01-1

MF C10 H20 N2 S4

CI COM  
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN\*, BIOBUSINESS, BIOSIS,  
BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CEN,  
CHEMCATS, CHEMINFORMRX, CHEMLIST, CHEMSAFE, CIN, CSCHEM, CSNB, DDFU,  
DIOGENES, DRUGU, DRUGUPDATES, EMBASE, GMELIN\*, HODOC\*, HSDB\*, IFICDB,  
IFIPAT, IFIUDB, IPA, MEDLINE, MRCK\*, MSDS-OHS, NIOSHTIC, PHARMASEARCH,  
PROMT, RTECS\*, SPECINFO, TOXCENTER, USAN, USPATFULL  
(\*File contains numerically searchable property data)  
Other Sources: DSL\*\*, EINECS\*\*, TSCA\*\*, WHO  
(\*\*Enter CHEMLIST File for up-to-date regulatory information)



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2152 REFERENCES IN FILE CA (1967 TO DATE)  
42 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
2156 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 137:74566  
REFERENCE 2: 137:73615  
REFERENCE 3: 137:63538  
REFERENCE 4: 137:47787  
REFERENCE 5: 137:34375  
REFERENCE 6: 137:1669  
REFERENCE 7: 136:402082  
REFERENCE 8: 136:384227  
REFERENCE 9: 136:379617  
REFERENCE 10: 136:359716

L8 ANSWER 11 OF 12 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1964:464408 CAPLUS

DOCUMENT NUMBER: 61:64408

ORIGINAL REFERENCE NO.: 61:11193e-f

TITLE: Development and application of fungistatic compounds  
for treatment of **cancer**

AUTHOR(S): Nieper, Hans A.; Xalabarder, Conrado

CORPORATE SOURCE: Krankenhaus, Aschaffenburg, Germany

SOURCE: Aerzt. Forsch. (1962), 16, I/523-I/540

DOCUMENT TYPE: Journal

LANGUAGE: German

AB The fungistatic substances were first tested in vitro on fungi and yeasts, esp. on *Candida tropicalis*, then on **tumors** (Ehrlich ascites carcinoma) and on **tumor** cells. Compds. contg. hydroxymethyl groups, ethylenimine groups, and S were compared for their effectiveness as antioncogenic agents. Trioxymethyl melanin proved still to be a most effective agent. Synthetic bis(hydroxymethylthiocarbamoyl) disulfide (LK 92) and compds. of related structure gave promising results.

IT Neoplasms

(inhibitors of, fungicides as)

IT Disulfide, bis[(3-carboxypiperidino)thiocarbonyl](?)

Glucitol, 1,1'-[dithiobis[(thiocarbonyl)(methylimino)]]bis[1-deoxy-

Thiuram disulfide bis(arginyl)-, bis(glucosamine)-

Thiuram disulfide bis(arginyl)-, bis(hydroxymethyl)-

(as neoplasm inhibitor)

IT 94-37-1, Disulfide, bis(piperidinethiocarbonyl) **729-46-4**,

Disulfide, bis(morpholinethiocarbonyl) 3562-31-0, Disulfide,

bis[(hydroxymethyl)thiocarbamoyl] 4310-59-2, D-Glucose,

2,2'-[dithiobis[(thiocarbonyl)imino]]bis[2-deoxy- 90114-66-2, Disulfide,

bis[methyl(D-gluc-2,3,4,5,6-pentahydroxyhexyl)thiocarbamoyl]

93896-57-2, Nipecotic acid, 1,1'-[dithiobis(thiocarbonyl)]di-(?)

97771-69-2, Disulfide, bis[methyl(2-morpholinoethyl)thiocarbamoyl]

(as neoplasm inhibitor)

IT 1017-56-7, Methanol, (s-triazine-2,4,6-triyltriimino)tri-

(neoplasm inhibition and)



ACCESSION NUMBER: 1999:507293 CAPLUS

DOCUMENT NUMBER: 132:87659

TITLE: Potential drugs against **cervical cancer**: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein

AUTHOR(S): Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.

CORPORATE SOURCE: Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore

SOURCE: Journal of the National Cancer Institute (1999), 91(14), 1211-1220

CODEN: JNCIEQ; ISSN: 0027-8874

PUBLISHER: Oxford University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The principal agent in the etiol. of **cervical cancer**, i.e., human **papillomavirus** (HPV) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of HPV -contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic HPV -contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of HPV. These assay systems may be useful in the development of drugs against **cervical cancer**, genital **warts**, and asymptomatic infections by genital **HPVs**.

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E5; potential drugs against **cervical cancer**)

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E6; potential drugs against **cervical cancer**)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(E7; potential drugs against **cervical cancer**)

IT Antiviral agents

(anti- **HPV**; potential drugs against **cervical cancer**)

IT Uterus, neoplasm

Uterus, neoplasm  
(cervix, inhibitors; potential drugs against **cervical cancer**)

IT Antitumor agents  
(cervix; potential drugs against **cervical cancer**)

IT Analysis  
Apoptosis  
Drug design  
Drug screening  
Human **papillomavirus**  
Redox reaction  
(potential drugs against **cervical cancer**)

IT p53 (protein)  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(potential drugs against **cervical cancer**)

IT Fusion proteins (chimeric proteins)  
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)  
(potential drugs against **cervical cancer**)

IT 56-17-7, Cystamine dihydrochloride 56-89-3, Cystine, analysis 69-78-3  
97-77-8, Tetraethylthiuram disulfide 100-32-3 103-33-3, Azobenzene  
**103-34-4** 119-80-2 120-78-5, 2,2'-Dithiobis(benzothiazole)  
123-77-3, Azodicarbonamide 135-57-9, Bis(2-benzamidophenyl)disulfide  
150-60-7, Dibenzyl disulfide 537-91-7, Bis(3-Nitrophenyl)disulfide  
586-96-9, Nitrosobenzene 644-32-6, Benzoyl disulfide 870-93-9,  
DL-Homocystine 882-33-7, Phenyl disulfide 940-69-2, .alpha.-Lipoamide  
1141-88-4, 2,2'-Dithiodianiline 1155-00-6, Bis(2-nitrophenyl)disulfide  
1160-68-5 2127-03-9, Aldrithiol 2 5398-51-6 13895-38-0,  
4-Nitrosoresorcinol-1-monomethyl ether 15441-06-2, 3,3'-  
Dithiodipropionic acid dimethyl ester 16766-09-9, Bis(4-Acetamidophenyl)disulfide 26907-82-4 47231-30-1 108872-98-6  
120586-49-4, 1,2-Dithiane-4,5-diol, 1,1-dioxide, cis 207802-09-3  
RL: ANT (Analyte); ANST (Analytical study)  
(potential drugs against **cervical cancer**)

IT 7440-66-6, Zinc, biological studies 50812-37-8, Glutathione  
S-transferase  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(potential drugs against **cervical cancer**)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS  
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:175791 CAPLUS

DOCUMENT NUMBER: 132:222549

TITLE: Preparation of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders

INVENTOR(S): Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui

PATENT ASSIGNEE(S): Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014063	A1	20000316	WO 1999-AU724	19990903
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
CA 2342858	AA	20000316	CA 1999-2342858	19990903
AU 9958401	A1	20000327	AU 1999-58401	19990903
EP 1112250	A1	20010704	EP 1999-945758	19990903
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
JP 2002524442	T2	20020806	JP 2000-568822	19990903
PRIORITY APPLN. INFO.:			AU 1998-5733	A 19980904
			AU 1999-1645	A 19990715
			WO 1999-AU724	W 19990903
OTHER SOURCE(S):	MARPAT 132:222549			
AB	R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoreq.2; n = 1-5], inhibitors of proteins encoded by an <b>MPV</b> gene by disruption of a chelated metal cation domain, were prepd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prepd. Data for biol. activity of I were given.			
IT	Proteins, specific or class			
RL:	BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)			
	(E6; prepn. of bis(piperazinyl) disulfides and analogs for treatment of <b>papillomavirus</b> -mediated disorders)			
IT	Transcription factors			
RL:	BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)			
	(E7; prepn. of bis(piperazinyl) disulfides and analogs for treatment of <b>papillomavirus</b> -mediated disorders)			
IT	Uterus, neoplasm			
	Uterus, neoplasm			
	(cervix, inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of <b>papillomavirus</b> -mediated disorders)			
IT	Antitumor agents			

(cervix; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Transforming proteins  
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
 (inhibitors; prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT Human **papillomavirus** 16  
 Human **papillomavirus** 18  
**Papillomavirus**  
 (prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

IT 103-34-4P 729-46-4P 1623-84-3P  
 1623-85-4P 2759-28-6DP, N-Benzylpiperazine, 4,4'-polythiobis deriv. 6542-61-6P 7764-30-9P 10220-20-9P  
 15575-30-1P 26087-98-9P 35386-24-4DP,  
 1-(2-Methoxyphenyl)piperazine, 4,4'-polythiobis deriv. 36938-10-0P  
 59226-72-1P 85865-96-9P 98999-00-9P  
 260973-66-8P 260973-68-0P 260973-72-6P 260973-74-8P  
 260973-75-9P 260973-76-0P 260973-79-3P 260973-81-7P  
 260973-83-9P 260973-85-1P 260973-87-3P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:840664 CAPLUS

DOCUMENT NUMBER: 134:110110

TITLE: Inactivation of the human **papillomavirus-16**  
E6 oncoprotein by organic disulfides

AUTHOR(S): Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo;  
Bernard, Hans-Ulrich; Ting, Anthony E.

CORPORATE SOURCE: Drug Screen Development Laboratory, Institute of  
Molecular and Cell Biology, Singapore, 117609,  
Singapore

SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(11),  
2549-2560

CODEN: BMECEP; ISSN: 0968-0896

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB We are investigating compds. that could be useful in the treatment of  
neoplastic **lesions** of the cervix by acting on the oncoprotein E6  
of human **papillomavirus-16**. The E6 protein contains two  
potential zinc-binding domains that are required for most of its  
functions. We have published tests that measure (i) the release of zinc  
ions after chem. alteration of the cysteine groups of these zinc-binding  
domains (TSQ assay), (ii) the interaction of E6 with the cellular proteins  
E6AP and E6BP (BIACORE assay), and (iii) the viability of **tumor**  
cell lines that require the continuous expression of **HPV**  
oncoproteins (WST1 assay). Based on these tests, we identified  
4,4'-dithiodimorpholine as a potential lead compd. In this study we  
examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be  
an important mol. prerequisite for further drug development in this  
system. We have evaluated 59 new substances including org. disulfides and  
those contg. the dithiobisamine moiety, as well as structural analogs.  
The compds. with significant reactivity in all three assays were obsd.  
only for dithiobisamine derivs. with satd. cyclic amines and aryl  
substituted piperazines. The identity of these substances suggests that  
the N-S-S-N moiety is necessary but not sufficient for reactivity in our  
assays, and that dithiobisamine based substances are useful as lead  
compds. that target the cysteine groups of **HPV-16** E6 zinc  
fingers.

IT Proteins, specific or class

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL  
(Biological study); PROC (Process)

(E6; prepn. of org. disulfides and inactivation of human  
**papillomavirus-16** E6 oncoprotein)

IT Uterus, neoplasm

(cervix, inhibitors; prepn. of org. disulfides and inactivation of  
human **papillomavirus-16** E6 oncoprotein)

IT Antitumor agents

(cervix; prepn. of org. disulfides and inactivation of human  
**papillomavirus-16** E6 oncoprotein)

IT Human **papillomavirus** 16

Structure-activity relationship

(prepn. of org. disulfides and inactivation of human  
**papillomavirus-16** E6 oncoprotein)

IT Amines, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(secondary; prepn. of org. disulfides and inactivation of human  
**papillomavirus-16** E6 oncoprotein)

IT Protein motifs

(zinc-binding domain; prepn. of org. disulfides and inactivation of  
human **papillomavirus-16** E6 oncoprotein)

IT 729-46-4P 1013-93-0P 1468-28-6P 2129-27-3P

5328-68-7P 6542-61-6P 7764-30-9P 10220-20-9P  
 15575-30-1P 16131-50-3P 17376-42-0P 36903-85-2P  
 36938-10-0P 59226-72-1P 62158-06-9P  
 72896-38-9P 85865-96-9P 98999-00-9P  
 103388-17-6P 260973-66-8P 260973-72-6P  
 260973-79-3P 260973-81-7P 260973-83-9P  
 260973-85-1P 303796-55-6P 320609-04-9P 320609-05-0P  
 320609-06-1P 320609-07-2P 320609-08-3P  
 320609-09-4P 320609-10-7P 320609-11-8P  
 320609-12-9P 320609-13-0P 320609-14-1P 320609-15-2P  
 320609-16-3P 320609-17-4P 320609-18-5P  
 320609-19-6P 320609-21-0P 320609-22-1P  
 320609-23-2P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of org. disulfides and inactivation of human  
**papillomavirus-16 E6 oncoprotein**)

IT 103-34-4 120-78-5 880-09-1 1623-84-3  
 1623-85-4 2127-10-8 2550-40-5 3256-06-2,  
 Thioperoxydicarbonimidic diamide ( $[(H_2N)C(NH)]_2S_2$ ) 5117-07-7  
 14193-38-5 15658-35-2 26087-98-9 61747-35-1 66304-01-6  
 66546-28-9

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(prepn. of org. disulfides and inactivation of human  
**papillomavirus-16 E6 oncoprotein**)

IT 85-46-1, Naphthalene-1-sulfonyl chloride 98-88-4, Benzoyl chloride  
 110-91-8, Morpholine, reactions 1122-82-3, Cyclohexyl isothiocyanate  
 6160-65-2, 1,1'-Thiocarbonyl diimidazole 7693-46-1, 4-Nitrophenyl  
 chloroformate 10025-67-9, Disulfur dichloride

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of org. disulfides and inactivation of human  
**papillomavirus-16 E6 oncoprotein**)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS  
 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB We are investigating compds. that could be useful in the treatment of neoplastic **lesions** of the cervix by acting on the oncoprotein E6 of human **papillomavirus**-16. The E6 protein contains two potential zinc-binding domains that are required for most of its functions. We have published tests that measure (i) the release of zinc ions after chem. alteration of the cysteine groups of these zinc-binding domains (TSQ assay), (ii) the interaction of E6 with the cellular proteins E6AP and E6BP (BIACORE assay), and (iii) the viability of **tumor** cell lines that require the continuous expression of **HPV** oncoproteins (WST1 assay). Based on these tests, we identified 4,4'-dithiodimorpholine as a potential lead compd. In this study we examd. whether the dithiobisamine moiety of 4,4'-dithiodimorpholine may be an important mol. prerequisite for further drug development in this system. We have evaluated 59 new substances including org. disulfides and those contg. the dithiobisamine moiety, as well as structural analogs. The compds. with significant reactivity in all three assays were obsd. only for dithiobisamine derivs. with satd. cyclic amines and aryl substituted piperazines. The identity of these substances suggests that the N-S-S-N moiety is necessary but not sufficient for reactivity in our assays, and that dithiobisamine based substances are useful as lead compds. that target the cysteine groups of **HPV**-16 E6 zinc fingers.

ACCESSION NUMBER: 2000:840664 CAPLUS  
DOCUMENT NUMBER: 134:110110  
TITLE: Inactivation of the human **papillomavirus**-16  
E6 oncoprotein by organic disulfides  
AUTHOR(S): Beerheide, Walter; Sim, Mui Mui; Tan, Yee-Joo;  
Bernard, Hans-Ulrich; Ting, Anthony E.  
CORPORATE SOURCE: Drug Screen Development Laboratory, Institute of  
Molecular and Cell Biology, Singapore, 117609,  
Singapore  
SOURCE: Bioorganic & Medicinal Chemistry (2000), 8(11),  
2549-2560  
CODEN: BMECEP; ISSN: 0968-0896  
PUBLISHER: Elsevier Science Ltd.  
DOCUMENT TYPE: Journal  
LANGUAGE: English

RE

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L8 ANSWER 3 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB R1R2NZSSnZNR3R4 (I) [R1-R4 = H, alkyl, acyl, aryl, etc.; R1R2,R3R4 = (CH2)lUm(CH2)p; U = bond, O, S, NH, CH2; Z = bond or where n = 1 Z may = CS; l,p = 0-6; m = 0 or 1; l+m+p.gtoeq.2; n = 1-5], inhibitors of proteins encoded by an **MPV** gene by disruption of a chelated metal cation domain, were prepd. Thus, e.g., R1R2NSSNR3R4 (R1R2,R3R4 = CH2CH2NRCH2CH2, R = 2-pyridinyl) was prepd. Data for biol. activity of I were given.

ACCESSION NUMBER: 2000:175791 CAPLUS

DOCUMENT NUMBER: 132:222549

TITLE: Preparation of bis(piperazinyl) disulfides and analogs for treatment of **papillomavirus**-mediated disorders

INVENTOR(S): Bernard, Hans-Ulrich; Tan, Yee Joo; Beerheide, Walter; Ting, Anthony Eugene; Sim, Mui Mui

PATENT ASSIGNEE(S): Institute of Molecular & Cell Biology, Singapore; Hughes, E. John L.

SOURCE: PCT Int. Appl., 78 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000014063	A1	20000316	WO 1999-AU724	19990903
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,				



KG, KZ, MD, RU, TJ, TM  
 RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK,  
 ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,  
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  
 CA 2342858 AA 20000316 CA 1999-2342858 19990903  
 AU 9958401 A1 20000327 AU 1999-58401 19990903  
 EP 1112250 A1 20010704 EP 1999-945758 19990903  
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,  
 IE, SI, LT, LV, FI, RO  
 JP 2002524442 T2 20020806 JP 2000-568822 19990903  
 PRIORITY APPLN. INFO.: AU 1998-5733 A 19980904  
 AU 1999-1645 A 19990715  
 WO 1999-AU724 W 19990903

OTHER SOURCE(S): MARPAT 132:222549

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L8 ANSWER 4 OF 12 CAPLUS COPYRIGHT 2003 ACS

AB The principal agent in the etiol. of **cervical cancer**, i.e., human **papillomavirus (HPV)** type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of **HPV**-contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic **HPV**-contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol.

and pathol. of HPV. These assay systems may be useful in the development of drugs against **cervical cancer**, genital **warts**, and asymptomatic infections by genital HPVs.

ACCESSION NUMBER: 1999:507293 CAPLUS  
DOCUMENT NUMBER: 132:87659  
TITLE: Potential drugs against **cervical cancer**: zinc-ejecting inhibitors of the human **papillomavirus** type 16 E6 oncoprotein  
AUTHOR(S): Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.  
CORPORATE SOURCE: Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore  
SOURCE: Journal of the National Cancer Institute (1999), 91(14), 1211-1220  
CODEN: JNCIEQ; ISSN: 0027-8874  
PUBLISHER: Oxford University Press  
DOCUMENT TYPE: Journal  
LANGUAGE: English

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9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1990:92775 CAPLUS

DN 112:92775

TI The E6 and E7 genes of HPV-18 are sufficient for inducing two-stage in vitro transformation of human keratinocytes

AU Barbosa, Miguel S.; Schlegel, Richard

CS Lab. Cell. Oncol., Natl. Cancer Inst., Bethesda, MD, 20892, USA

SO Oncogene (1989), 4(12), 1529-32

CODEN: ONCNES; ISSN: 0950-9232

DT Journal

LA English

AB Using a recently described keratinocyte assay, HPV-18 DNA was shown to induce 2 progressive steps in cellular transformation (a large cell and a small cell stage). Both steps of this keratinocyte transformation can be achieved with a subgenomic fragment contg. only the HPV-18 regulatory region and E6/E7 genes. Similar to cell lines transformed by the complete HPV-18 genome, keratinocytes transformed by the HPV-18 E6/E7 genes express the major early viral protein (E7) but are non-tumorigenic in nude mice. Interestingly, HPV-18 DNA was noted to be 5 times more efficient than HPV-16 DNA for in vitro keratinocyte transformation, regardless of the method of DNA transfection.

=>

L10 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1999:507293 CAPLUS

DN 132:87659

TI Potential drugs against cervical cancer: zinc-ejecting inhibitors of the human papillomavirus type 16 E6 oncoprotein

AU Beerheide, Walter; Bernard, Hans-Ulrich; Tan, Yee-Joo; Ganesan, Arasu; Rice, William G.; Ting, Anthony E.

CS Screening for Novel Inhibitors Laboratory, Institute of Molecular and Cell Biology, Singapore, 117609, Singapore

SO Journal of the National Cancer Institute (1999), 91(14), 1211-1220

CODEN: JNCIEQ; ISSN: 0027-8874

PB Oxford University Press

DT Journal

LA English

AB The principal agent in the etiol. of cervical cancer, i.e., human papillomavirus (HPV) type 16, encodes three oncoproteins, E5, E6, and E7. Structural and mutational studies have identified two potential zinc-finger domains as crit. for E6 protein function. We investigated several assays to identify and characterize compds. that interfere with the binding of zinc to E6. Thirty-six compds. were selected on the basis of their structure, which would facilitate their participation in sulfhydryl residue-specific redox reactions, and were tested for their ability to release zinc from E6 protein. The zinc-ejecting compds. were then tested for their ability to inhibit E6 binding to E6-assocd. protein (E6AP) and E6-binding protein (E6BP), two coactivators of E6-mediated cellular transformation. The binding of E6 to E6BP and E6AP was measured by use of surface plasmon resonance (a technique that monitors mol. interactions by measuring changes in refractive index) and by use of in vitro translation assays. The compds. were also tested for their effects on the viability of HPV-contg. cell lines. Nine of the 36 tested compds. ejected zinc from E6. Two of the nine compds. inhibited the interaction of E6 with E6AP and E6BP, and one of these two, 4,4'-dithiodimorpholine, selectively inhibited cell viability and induced higher levels of p53 protein (assocd. with the induction of apoptosis [programmed cell death]) in tumorigenic HPV-contg. cells. We have described assay systems to identify compds., such as 4,4'-dithiodimorpholine, that can potentially interfere with the biol. and pathol. of HPV. These assay systems may be useful in the development of drugs against cervical cancer, genital warts, and asymptomatic infections by genital HPVs.

RE.CNT 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1980:69670 CAPLUS

DN 92:69670

TI Inhibition of cis-platinum nephrotoxicity by diethyldithiocarbamate rescue in a rat model

AU Borch, Richard F.; Pleasants, Michael E.

CS Dep. Chem., Univ. Minnesota, Minneapolis, MN, 55455, USA

SO Proceedings of the National Academy of Sciences of the United States of America (1979), 76(12), 6611-14

CODEN: PNASA6; ISSN: 0027-8424

DT Journal

LA English

AB The nephrotoxic effects of cis-dichlorodiammineplatinum(II) (NSC-119875) [15663-27-1] administered to male F344 rats at the median LD (LD50; 7.5 mg/kg) were inhibited by treatment with Na diethyldithiocarbamate [148-18-5] (500 or 750 mg/kg) between 1 and 4 h after cis-platinum administration. Those animals receiving cis-platinum alone had mean serum blood urea N levels of 234 mg/dl at the time of maximal toxicity. When dithiocarbamate rescue was carried out after cis-platinum treatment, mean blood urea N levels were 56-95 mg/dl; kidney sections were grossly normal with a barely discernible band of degeneration at the corticomedullary junction. Gastrointestinal toxicity was obsd. in >95% of the cis-platinum-treated rats but was totally absent in those receiving subsequent rescue treatment. A significant decrease in wt. loss was also obsd. in the dithiocarbamate-rescued rats. Based on the chem. of platinum-sulfur interactions and the obsd. time-dependence of the rescue treatment, it is suggested that dithiocarbamate exerts its effects via competitive chelation and removal of Pt coordinated to protein-bound SH groups of the kidney tubule cells.

AN 1995:434468 CAPLUS  
 DN 122:210936  
 TI Functional p53 protein in human papillomavirus-positive cancer cells  
 AU Butz, Karin; Shahabeddin, Lili; Geisen, Caroline; Spitkovsky, Dimitry;  
 Ullmann, Angela; Hoppe-Seyler, Felix  
 CS Projektgruppe Angewandte Tumorstudiologie, Deutsches Krebsforschungszentrum,  
 Heidelberg, D-69120, Germany  
 SO Oncogene (1995), 10(5), 927-36  
 CODEN: ONCNES; ISSN: 0950-9232  
 PB Stockton  
 DT Journal  
 LA English  
 AB There is accumulating evidence that the p53 protein contributes to tumor  
 suppression by stimulating the transcription of specific cellular genes,  
 such as the cell cycle control gene WAF1/C1P1. P53-mediated  
 transcriptional activation is inhibited in cotransfection assays by  
 overexpressed E6 protein from cancer-assocd. human papillomavirus (HPV)  
 types, pointing at a possible mol. mechanism by which these viruses  
 contribute to malignant cell transformation. Here we analyzed the  
 transcriptional transactivation function of endogenous p53 protein in a  
 series of cervical cancer cell lines, which express the E6 gene from  
 integrated viral sequences. Transient and stable transfection analyses  
 employing p53-responsive reporter constructs indicated that HPV-pos.  
 cervical cancer cells contained transactivating p53 protein. Treatment of  
 HPV-pos. cells with genotoxic agents, such as mitomycin C, cisplatin, or  
 u.v. irradiation, resulted in an increase of nuclear p53 protein levels and  
 enhanced binding of p53 to a p53-recognition site. These effects were  
 accompanied by an increase of WAF1/C1P1 mRNA levels. In several HPV-pos.  
 cell lines, these mol. events were linked to a cell cycle arrest in G1.  
 In contrast, cancer cells containing mutant p53 genes did not contain  
 transactivating endogenous p53 protein and lacked the p53-mediated  
 response to DNA damaging agents. These results indicate that the  
 tumorigenic phenotype of HPV-pos. cancer cell lines does not necessarily  
 correlate with a lack of basal or DNA damage induced p53 activities and  
 that therefore the presence of high risk HPV sequences is not functionally  
 equivalent to the loss of p53 function through somatic mutations of the p53  
 gene.

AN 1995:502169 CAPLUS  
 DN 123:76166  
 TI Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy  
 AU Chan, Shih-Yen; Delius, Hajo; Halpern, Aaron L.; Bernard, Hans-Ulrich  
 CS Institute of Molecular and Cell Biology, National University of Singapore, Singapore, 0511, Singapore  
 SO Journal of Virology (1995), 69(5), 3074-83  
 CODEN: JOVIAM; ISSN: 0022-538X  
 PB American Society for Microbiology  
 DT Journal  
 LA English  
 AB Our aim was to study the phylogenetic relationships of all known papillomaviruses (PVs) and the possibility of establishing a supratype taxonomic classification based on this information. Of the many detectably homologous segments present in PV genomes, a 291-bp segment of the L1 gene is notable because it is flanked by the MY09 and MY11 consensus primers and contains highly conserved amino acid residues which simplify sequence alignment. We detd. the MY09-MY11 sequences of human PV type 20 (HPV-20), HPV-21, HPV-22, HPV-23, HPV-24, HPV-36, HPV-37, HPV-38, HPV-48, HPV-50, HPV-60, HPV-70, HPV-72, HPV-73, ovine (sheep) PV, bovine PV type 3 (BPV-3), BPV-5, and BPV-6 and created a database which now encompasses HPV-1 to HPV-70, HPV-72, HPV-73, seven yet untyped HPV genomes, and 15 animal PV types. Three addnl. animal PVs were analyzed on the basis of other sequence data. We constructed phylogenies based on partial L1 and E6 gene sequences and distinguished five major clades that call supergroups. One of them unites 54 genital PV types, which can be further divided into eleven groups. The second supergroup has 24 types and unites most PVs that are typically found in epidermodysplasia verruciformis patients but also includes several types typical of other cutaneous lesions, like HPV-4. The third supergroup unites the six known ungulate fibropapillomaviruses, the fourth includes the cutaneous ungulate PVs BPV-3, BPV-4, and BPV-6, and the fifth includes HPV-1, HPV-41, HPV-63, the canine oral PV, and the cottontail rabbit PV. The chaffinch PV and two rodent PVs, *Micromys minutus* PV and *Mastomys natalensis* PV, are left ungrouped because of the relative isolation of each of their lineages. Within most supergroups, groups formed on the basis of cladistic principles unite phenotypically similar PV types. We discuss the basis of our classification, the concept of the PV type, speciation, PV-ho



AN 1995:502169 CAPLUS  
 DN 123:76166  
 TI Analysis of genomic sequences of 95 papillomavirus types: uniting typing, phylogeny, and taxonomy  
 AU Chan, Shih-Yen; Delius, Hajo; Halpern, Aaron L.; Bernard, Hans-Ulrich  
 CS Institute of Molecular and Cell Biology, National University of Singapore, Singapore, 0511, Singapore  
 SO Journal of Virology (1995), 69(5), 3074-83  
 CODEN: JOVIAM; ISSN: 0022-538X  
 PB American Society for Microbiology  
 DT Journal  
 LA English  
 AB Our aim was to study the phylogenetic relationships of all known papillomaviruses (PVs) and the possibility of establishing a supratype taxonomic classification based on this information. Of the many detectably homologous segments present in PV genomes, a 291-bp segment of the L1 gene is notable because it is flanked by the MY09 and MY11 consensus primers and contains highly conserved amino acid residues which simplify sequence alignment. We detd. the MY09-MY11 sequences of human PV type 20 (HPV-20), HPV-21, HPV-22, HPV-23, HPV-24, HPV-36, HPV-37, HPV-38, HPV-48, HPV-50, HPV-60, HPV-70, HPV-72, HPV-73, ovine (sheep) PV, bovine PV type 3 (BPV-3), BPV-5, and BPV-6 and created a database which now encompasses HPV-1 to HPV-70, HPV-72, HPV-73, seven yet untyped HPV genomes, and 15 animal PV types. Three addnl. animal PVs were analyzed on the basis of other sequence data. We constructed phylogenies based on partial L1 and E6 gene sequences and distinguished five major clades that call supergroups. One of them unites 54 genital PV types, which can be further divided into eleven groups. The second supergroup has 24 types and unites most PVs that are typically found in epidermodysplasia verruciformis patients but also includes several types typical of other cutaneous lesions, like HPV-4. The third supergroup unites the six known ungulate fibropapillomaviruses, the fourth includes the cutaneous ungulate PVs BPV-3, BPV-4, and BPV-6, and the fifth includes HPV-1, HPV-41, HPV-63, the canine oral PV, and the cottontail rabbit PV. The chaffinch PV and two rodent PVs, *Micromys minutus* PV and *Mastomys natalensis* PV, are left ungrouped because of the relative isolation of each of their lineages. Within most supergroups, groups formed on the basis of cladistic principles unite phenotypically similar PV types. We discuss the basis of our classification, the concept of the PV type, speciation, PV-host evolution, and ests. of their rates of evolution.

AN 1995:719736 CAPLUS

DN 123:195281

TI Interaction of papillomavirus E6 oncoproteins with a putative calcium-binding protein

AU Chen, Jason J.; Reid, Carl E.; Band, Vimla; Androphy, Elliot J.

CS Sch. Med., Tufts Univ., Boston, MA, 02111, USA

SO Science (Washington, D. C.) (1995), 269(5223), 529-31

CODEN: SCIEAS; ISSN: 0036-8075

PB American Association for the Advancement of Science

DT Journal

LA English

AB Human papillomaviruses (HPVs) are assocd. with the majority of cervical cancers and encode a transforming protein, E6, that interacts with the tumor suppressor protein p53. Because E6 has p53-independent transforming activity, the yeast two-hybrid system was used to search for other E6-binding proteins. One such protein, E6BP, interacted with cancer-assocd. HPV E6 and with bovine papillomavirus type 1 (BPV-1) E6. The transforming activity of BPV-1 E6 mutants correlated with their E6BP-binding ability. E6BP is identical to a putative calcium-binding protein, ERC-55, that appears to be localized in the endoplasmic reticulum.

AN 1992:609888 CAPLUS  
DN 117:209888  
TI Degradation of p53 can be targeted by HPV E6 sequences distinct from those required for p53 binding and trans-activation  
AU Crook, Tim; Tidy, John A.; Vousden, Karen H.  
CS Med. Sch., St. Mary's Hosp., London, W2 1PG, UK  
SO Cell (Cambridge, MA, United States) (1991), 67(3), 547-56  
CODEN: CELLB5; ISSN: 0092-8674  
DT Journal  
LA English  
AB Human papillomavirus (HPV) types 16 and 18 appear to play a role in the development of ano-genital malignancies, whereas HPV 6 and 11 are usually assocd. with benign lesions. One HPV 16 oncoprotein, E6, complexes with and promotes degrdn. of the cellular tumor suppressor p53. Here the authors show that E6 proteins of both oncogenic and benign HPV types assoc. in vitro with p53, but binding by E6 proteins of benign HPV types cannot target p53 for degrdn. A C-terminal region of E6 conserved among all HPV types is important for p53 binding. However, N-terminal sequences of E6 conserved only between oncogenic HPV types are necessary to direct p53 degrdn. P53 binding by E6 appears necessary but not sufficient for this activity. All E6 proteins tested showed comparable transcriptional trans-activating activity, a property that does not require the ability to bind or direct degrdn. of p53.

AN 1989:171017 CAPLUS

DN 110:171017

TI The human papilloma virus-16 E7 oncoprotein is able to bind to the retinoblastoma gene product

AU Dyson, Nicholas; Howley, Peter M.; Muenger, Karl; Harlow, Ed

CS Cold Spring Harbor Lab., Spring Harbor, NY, 11724, USA

SO Science (Washington, DC, United States) (1989), 243(4893), 934-7

CODEN: SCIEAS; ISSN: 0036-8075

DT Journal

LA English

AB Deletions or mutations of the retinoblastoma gene, RB1, are common features of many tumors and tumor cell lines. Recently, the RB1 gene product, p105-RB, has been shown to form stable protein/protein complexes with oncoproteins of 2 DNA tumor viruses, the adenovirus E1A proteins and the simian virus 40 (SV40) large T antigen. Neither of these viruses is thought to be assocd. with human cancer, but they can cause tumors in rodents. Binding between the RB anti-oncoprotein and the adenovirus or SV40 oncoprotein can be recapitulated in vitro with coimmunopptn. mixing assays. These assays have been used to demonstrate that the E7 oncoprotein of the human papilloma virus type 16 can form similar complexes with p105-RB. Human papilloma virus 16 is found assocd. with approx. 50 percent of cervical carcinomas. These 3 DNA viruses may utilized similar mechanisms in transformation. The results implicate RB binding as a possible step in human papilloma virus-assocd. carcinogenesis.

L17 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2003 ACS

AN 1995:244480 CAPLUS

DN 122:95783

TI Comparative studies on the pharmacokinetics of hydrophilic prolinedithiocarbamate, sarcosinedithiocarbamate and the less hydrophilic diethyldithiocarbamate

AU Frank, N.; Christmann, A.; Frei, E.

CS German Cancer Research Center, Division of Molecular Toxicology, Im Neuenheimer Feld 280, Heidelberg, 69120, Germany

SO Toxicology (1995), 95(1-3), 113-22

CODEN: TXCYAC; ISSN: 0300-483X

PB Elsevier

DT Journal

LA English

AB The pharmacokinetics of the antitoxic and anticarcinogenic compds. diethyldithiocarbamate, prolinedithiocarbamate and sarcosinedithiocarbamate were compared in rats. The bioavailability, the distribution in the organism, the oxidn. to thiuramdisulfides, the cleavage to CS<sub>2</sub> and the excretion in urine and bile were investigated. The results showed different behavior of the three compds. The more toxic diethyldithiocarbamate had a short in vivo half-life, was oxidized to tetraethylthiuramdisulfide in blood, and was metabolized to high yields of CS<sub>2</sub> in 24 h. In contrast, prolinedithiocarbamate was more stable in vivo, was found predominantly in the urinary tract and was excreted in urine. The differences could not be explained by the presence of the carboxy group in the latter dithiocarbamate, since sarcosinedithiocarbamate, which also contains a carboxy group, behaved like diethyldithiocarbamate.

AN 1993:139404 CAPLUS  
DN 118:139404  
TI Induction of nuclear accumulation of the tumor-suppressor protein p53 by  
DNA-damaging agents  
AU Fritsche, Michael; Haessler, Christel; Brandner, Gerhard  
CS Inst. Med. Mikrobiol. Hyg., Univ. Freiburg, Freiburg, Germany  
SO Oncogene (1993), 8(2), 307-18  
CODEN: ONCNES; ISSN: 0950-9232  
DT Journal  
LA English  
AB Cancer therapy drugs, such as cisplatin, mitomycin C, etoposide and other  
comps., and energy-rich radiation act on cellular DNA. These agents  
induce nuclear accumulation of the tumor-suppressor protein p53 in  
fibroblastoid cells, as well as in epithelioid normal and immortalized  
cells of murine, simian, and human origin. The p53 accumulation starts a  
few hours after treatment and is detectable in surviving cells for at  
least 20 days. The accumulation occurs because of increased p53 protein  
stability and depends on ongoing translocation. It is not the result of  
enhanced gene expression. A no. of cell cycle inhibitors do not affect  
the p53 protein accumulation, suggesting that the process may start from  
several points in the cell cycle. Since the increase in the nuclear p53  
protein levels occurs within a few hours in most normal diploid cells, it  
is unlikely that the accumulated p53 protein is derived from a mutated p53  
gene. The DNA damage-induced p53 accumulation may either inhibit cell  
growth, allowing DNA repair processes, or in the case of severe damage it  
can initiate apoptosis.

AN 1998:460697 CAPLUS  
 DN 129:173955  
 TI Basal and human papillomavirus E6 oncoprotein-induced degradation of Myc proteins by the ubiquitin pathway  
 AU Gross-Mesilaty, Shlomit; Reinstein, Eyal; Bercovich, Beatrice; Tobias, Karin E.; Schwartz, Alan L.; Kahana, Chaim; Ciechanover, Aaron  
 CS Department of Biochemistry and the Rappaport Family Institute for Research in the Medical Sciences, The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, 31096, Israel  
 SO Proceedings of the National Academy of Sciences of the United States of America (1998), 95(14), 8058-8063  
 CODEN: PNASA6; ISSN: 0027-8424  
 PB National Academy of Sciences  
 DT Journal  
 LA English  
 AB We have previously shown that the degrdn. of c-myc and N-myc in vitro is mediated by the ubiquitin system. However, the role of the system in targeting the myc proteins in vivo and the identity of the conjugating enzymes and possible ancillary proteins involved has remained obscure. Here we report that the degrdn. of the myc proteins in cells is inhibited by lactacystin and MG132, two inhibitors of the 20S proteasome. Inhibition is accompanied by accumulation of myc-ubiquitin conjugates. Dissection of the ancillary proteins involved revealed that the high-risk human papillomavirus oncoprotein E6-16 stimulates conjugation and subsequent degrdn. of the myc proteins in vitro. Expression of E6-16 in cells results in significant shortening of the t1/2 of the myc proteins with subsequent decrease in their cellular level. Anal. of the conjugating enzymes revealed that under basal conditions the proteins can be conjugated by two pairs of E2s and E3s-E2-14 kDa and E3.alpha. involved in the "N-end rule" pathway, and E2-F1 (UbcH7) and E3-Fos involved also in conjugation of c-Fos. In the presence of E6-16, a third pair, E2-F1 and E6-AP mediate conjugation of myc by means of a mechanism that appears to be similar to that involved in the targeting of p53, formation of a myc E6.E6-AP targeting complex. It is possible that in certain cells E6-mediated targeting of myc prevents myc-induced apoptosis and thus ensures maintenance of viral infection.  
 RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 ALL CITATIONS AVAILABLE IN THE RE FORMAT

AN 1993:142054 CAPLUS  
DN 118:142054  
TI Cloning and expression of the cDNA for E6-AP, a protein that mediates the interaction of the human papillomavirus E6 oncoprotein with p53  
AU Huibregtse, Jon M.; Scheffner, Martin; Howley, Peter M.  
CS Lab. Tumor Virus Biol., Natl. Cancer Inst., Bethesda, MD, 20892, USA  
SO Molecular and Cellular Biology (1993), 13(2), 775-84  
CODEN: MCEBD4; ISSN: 0270-7306  
DT Journal  
LA English  
AB The E6 oncoproteins of the cancer-assocd. or high-risk human papillomaviruses (HPVs) target the cellular p53 protein. The assocn. of E6 with p53 leads to the specific ubiquitination and degrdn. of p53 in vitro, suggesting a model by which E6 deregulates cell growth control by the elimination of the p53 tumor suppressor protein. Complex formation between E6 and p53 requires an addnl. cellular factor, designated E6-AP (E6-assocd. protein), which has a native and subunit mol. mass of approx. 100 kDa. Here the purifn. of E6-AP and the cloning of its corresponding cDNA, which contains a novel open reading frame encoding 865 amino acids is reported. E6-AP, translated in vitro, has the following properties: (i) it assoc. with wild-type p53 in the presence of the HPV16 E6 protein and simultaneously stimulates the assocn. of E6 with p53, (ii) it assoc. with the high-risk HPV16 and HPV18 E6 proteins in the absence of p53, and (iii) induces the E6- and ubiquitin-dependent degrdn. of p53 in vitro.



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AN 1999:33268 CAPLUS

DN 130:208175

TI Inhibition of Bak-induced apoptosis by HPV-18 E6

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CS International Centre for Genetic Engineering and Biotechnology, Trieste,  
I-34012, Italy

SO Oncogene (1998), 17(23), 2943-2954

CODEN: ONCNES; ISSN: 0950-9232

PB Stockton Press

DT Journal

LA English

AB Human papillomavirus (HPV) E6 proteins inhibit apoptosis in both p53-dependent and p53-independent manners. A key point in apoptosis is the regulation provided by the Bcl-2 family; and in differentiating keratinocytes, in which HPV replicates, the Bak protein is highly expressed. The authors show that HPV-18 E6 will inhibit Bak-induced apoptosis and this is mediated by an interaction between the E6 and Bak proteins resulting in degrdn. of the Bak protein in vivo. The authors also show that Bak protein interacts with the ubiquitin ligase, E6AP, and that a mutant of Bak defective in E6AP binding is overexpressed in comparison with wild type. These studies suggest that Bak is probably the first naturally occurring target of E6AP to be identified.

RE.CNT 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD

ALL CITATIONS AVAILABLE IN THE RE FORMAT

N 1999:398754 CAPLUS

DN 131:168536

TI The human papillomavirus type 16 E6 gene alone is sufficient to induce carcinomas in transgenic animals

AU Song, Shiyu; Pitot, Henry C.; Lambert, Paul F.

CS McArdle Laboratory for Cancer Research, University of Wisconsin Medical School, Madison, WI, 53706, USA

SO Journal of Virology (1999), 73(7), 5887-5893

CODEN: JOVIAM; ISSN: 0022-538X

PB American Society for Microbiology

DT Journal

LA English

AB High-risk human papillomaviruses (HPVs) are the causative agents of certain human cancers. HPV type 16 (HPV16) is the papillomavirus most frequently assocd. with cervical cancer in women. The E6 and E7 genes of HPV are expressed in cells derived from these cancers and can transform cells in tissue culture. Animal expts. have demonstrated that E6 and E7 together cause tumors. The authors showed previously that E6 and E7 together or E7 alone could induce skin tumors in mice when these genes were expressed in the basal epithelia of the skin. In this study, the authors investigated the role that the E6 gene plays in carcinogenesis. The authors generated K14E6 transgenic mice, in which the HPV16 E6 gene was directed in its expression by the human keratin 14 promoter (hK14) to the basal layer of the epidermis. The authors found that E6 induced cellular hyperproliferation and epidermal hyperplasia and caused skin tumors in adult mice. Interestingly, the tumors derived from E6 were mostly malignant, as opposed to the tumors from E7 mice, which were mostly benign. This result leads the authors' to hypothesize that E6 may contribute differently than E7 to HPV-assocd. carcinogenesis; whereas E7 primarily contributes to the early stages of carcinogenesis that lead to the formation of benign tumors, E6 primarily contributes to the late stages of carcinogenesis that lead to malignancy.

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ALL CITATIONS AVAILABLE IN THE RE FORMAT

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